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HEREDITARY XANTHOMATOSIS

FAMILIAL INCIDENCE OF XANTHOMA TUBEROSUM ASSOCIATED WITH HYPERCHOLESTEREMIA AND CARDIOVASCULAR INVOLVEMENT, WITH REPORT OF SEVERAL CASES OF SUDDEN DEATH

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In accordance with the classification accepted by Thannhauser and Magendantz,[1] Montgomery [2] and other investigators, primary essential xanthomatosis may be divided into two main types, xanthoma tuberosum and xanthoma disseminatum. The distinction between these forms rests on a variety of clinical and biochemical differences, which concern the cholesterol content of the blood as well as the type and localization of the cutaneous and visceral lesions.

In xanthoma disseminatum there are numerous fine papules and plaques on the flexor surfaces of the extremities, especially in the axillary folds. The mucous membranes of the mouth, pharynx and larynx are often affected, and as a result of involvement of the pituitary gland there is frequent occurrence of diabetes insipidus. Thannhauser and Magendantz also associated with this disease involvement of the bones, lungs and brain and Schüller-Christian disease. The cholesterol content of the blood is usually normal in patients with this disease, which has been designated, therefore, "normocholesteremic."

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Read before the Section on Dermatology and Syphilology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

1. Thannhauser, S. J., and Magendantz, H.: The Different Clinical Groups of Xanthomatous Diseases: A Clinical Physiological Study of Twenty-Two Cases, Ann. Int. Med. **11**:1662 (March) 1938.

2. Montgomery, H.: Cutaneous Manifestations of Diseases of Lipoid Metabolism, M. Clin. North America **24**:1249 (July) 1940.

Xanthoma tuberosum is the type with which we are dealing in our family group. It is characterized by nodules, tumors and plaques, located predominantly on the elbows, knees and buttocks and over the achilles tendons and the tendons and joints of the fingers, toes, hands and feet. The cholesterol content of the blood is usually increased and has led to the classification of xanthoma tuberosum as "hypercholesteremic." Frequent association with cardiovascular disease is particularly significant.

Another distinguishing feature of xanthoma tuberosum appears to consist of its hereditary nature. Since familial occurrence of xanthoma disseminatum has been reported in only 1 case,[3] there is little doubt that the causes of the two forms differ significantly.

GENETIC ASPECTS OF XANTHOMA TUBEROSUM

The tendency of xanthoma tuberosum to occur in several members of a family has been known for a long time. Since the first observation of familial incidence by Wilks[4] in 1868, many families with accumulation of cutaneous xanthoma have been reported and numerous analyses of their taint have been made. Thirteen affected families were reviewed by Török,[5] in 1889, eighteen families by Morichau-Beauchant and Bessonnet,[6] in 1903, seven families by Gossage,[7] in 1908, thirty-three families with 103 affected persons by Fasold,[8] in 1924, and thirty-seven families with 114 affected members by Grenaud,[9] in 1927.

Török was the first to emphasize the hereditary nature of xanthoma, while Gossage classified the mode of its inheritance as single dominant. Incomplete dominance was assumed by Fasold in view of the fact that in nine of thirty-three families studied the parents of the affected siblings were free of cutaneous lesions, although they had descended from an affected grandparent or great-grandparent. A recessive mode of inheritance has been considered improbable, since no significant increase has been found in the frequency of consanguineous marriages among the

3. Mackenzie, S.: Two Cases of Congenital Xanthelasma, Tr. Path. Soc. London **33**:370, 1882.

4. Wilks, cited by Fagge, C. H.: Two Cases of Vitiligoidea Associated with Chronic Jaundice and Enlargement of the Liver, Tr. Path. Soc. London **19**:434, 1868.

5. Török, L.: De la nature des xanthomes (avec quelques remarques critiques sur la nature des tumeurs), Ann. de dermat. et syph. **4**:1109, 1893.

6. Morichau-Beauchant and Bessonnet, R.: Le xanthome héréditaire et familial, Arch. gén. de méd. **192**:2313, 1903.

7. Gossage, A. M.: The Inheritance of Certain Human Abnormalities, Quart. J. Med. **1**:331, 1908.

8. Fasold, A.: Studien über Vererbung von Hautkrankheiten: VI. Xanthom (Cholesterosis cutis), Arch. f. Rassen- u. Gesellsch.-Biol. **16**:54, 1924.

9. Grenaud, M.: Les xanthomes familiaux, Thesis, Paris, 1927.

parents of tainted siblings. Moreover, in some of the reported families the number of affected members has been so excessive as to preclude a recessive distribution of the trait. In the family reported on by Arning [10] the mother and 5 of her 9 children were affected; in the family described by Schmidt,[11] all 5 children; in the case of Llambias and Celesia,[12] the mother and 6 children; in the case of Hufschmitt,[13] 4 of 5 children, and in the family of Harbitz,[14] the father of an affected child and 6 of the paternal uncles.

The final analysis of the genetic mechanism producing xanthoma tuberosum is complicated by the observation that the main expression of the inheritable morbid factor may be constituted by a disturbance in the cholesterol metabolism rather than by the cutaneous lesions. This assumption has been substantiated by the observations in the family described by Schmidt, in which the parents of 5 children with cutaneous xanthomatosis were unaffected except for hypercholesteremia in the father, and by similar observations of Arndt,[15] Pautrier and Lévy,[16] Herrmann and Nathan,[17] Lapowski,[18] Weindel,[19] Lane and Goodman,[20] Sperry and Schick [21] and others.

Unfortunately, no determinations of the cholesterol content of the blood were made in most family cases in which the direct ancestors or descendants of trait carriers have been reported as unaffected. In the

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10. Arning, E.: Ein Fall von familiärer Xanthomatose, Arch. f. Dermat. u. Syph. **105**:290, 1910.

11. Schmidt, E.: Beiträge zur Xanthomfrage, Arch. f. Dermat. u. Syph. **140**: 408, 1922.

12. Llambias, J., and Celesia, A.: Xanthome familial, Compt. rend. Soc. de biol. **93**:1011, 1925.

13. Hufschmitt, M.: Un cas de xanthome familial, Presse méd. **32**:99 (Jan. 30) 1924.

14. Harbitz, F.: Tumors of Tendon Sheaths, Joint Capsules, and Multiple Xanthoma, Arch. Path. **4**:507 (Oct.) 1927.

15. Arndt, K. D.: Hereditäres, kongenitales, familiäres Xanthom, Zentralbl. f. Haut- u. Geschlechtskr. **7**:302, 1923.

16. Pautrier, M., and Lévy, G.: Trois cas de xanthomes en série familiale, avec infiltrations xanthomateuses tendineuses et juxtaarticulaires et hypercholesterinémie sanguine considérable, Presse méd. **31**:728, 1923.

17. Herrmann, F., and Nathan, E.: Zur Frage der Xanthomgenese, Arch. f. Dermat. u. Syph. **152**:575, 1926.

18. Lapowski, B.: Familial Xanthoma Tuberosum Multiplex in Two Sisters, Arch. Dermat. & Syph. **11**:701 (May) 1925.

19. Weindel, F.: Lidxanthoma und Hypercholesterinämie, Thesis, Munich, 1929.

20. Lane, G. C., and Goodman, J., Jr.: Xanthoma Tuberosum, Arch. Dermat. & Syph. **32**:377 (Sept.) 1935.

21. Sperry, W. M., and Schick, B.: Essential Xanthomatosis: Treatment with Cholesterol-Free Diet in Two Cases, Am. J. Dis. Child. **51**:1372 (June) 1936.

present state of knowledge, therefore, it is impossible to say definitely whether xanthoma or hypercholesteremia is inherited as the primary condition. It may be mentioned, however, that Polano [22] has tried to explain the irregular manifestation of xanthomatosis by assuming two different genetic factors, one for hypercholesteremia and one for cholesterophilia of cells.

ASSOCIATION OF XANTHOMA TUBEROSUM WITH HYPERCHOLESTEREMIA, CARDIOVASCULAR INVOLVEMENT AND SUDDEN DEATH

The association of xanthoma tuberosum with hypercholesteremia, cardiovascular involvement and sudden death has been observed by many investigators. In the case of xanthoma published by Fagge [23] necropsy revealed extensive involvement of the heart, aorta and other blood vessels, including the pulmonary arteries. In the case described by Fox [24] xanthoma was associated with mitral disease, while in the case of Poensgen [25] the aorta was found to be affected. Of the 2 siblings with xanthoma studied by Lehzen and Knauss [26] 1 had mitral insufficiency and died within twenty-four hours after a sudden attack of palpitation and shortness of breath. Necropsy revealed involvement of the coronary arteries, the mitral and aortic valves, the aorta, the carotid artery and pulmonary arteries. Sudden death was also reported by Gwynne [27] in 1 of 2 siblings affected by xanthoma.

In Arning's family suffering from xanthoma 3 siblings died suddenly of heart failure, at the ages of 16, 21 and 26 respectively, 2 of them while dancing. Hess [28] reported the case of a girl in whom xanthoma tuberosum developed at the age of 7 years and who died, at the age of 19, of acute cardiac failure within thirty-six hours. Necropsy showed involvement of the ostiums of the coronary arteries, the aortic valves, the aorta and most of the abdominal arteries. Sudden death likewise occurred in Harbitz' case of a man aged 38 who was affected by

22. Polano, M. K.: Ueber die Pathogenese der Cholesterosen der Haut, Arch. f. Dermat. u. Syph. **174**:213, 1936.

23. Fagge, C. H.: Xanthomatous Diseases of the Skin: I. General Xanthelasma or Vitiligoidea, Tr. Path. Soc. London **24**:242, 1873.

24. Fox, C.: A Case of Xanthelasma Multiplex, Lancet **2**:688 (Nov. 8) 1879.

25. Poensgen, A.: Mitteilung eines seltenen Falles von Xanthelasma multiplex, Virchows Arch. f. path. Anat. **91**:350, 1883.

26. Lehzen, G., and Knauss, K.: Ueber Xanthoma multiplex, planum, tuberosum, mollusciforme, Virchows Arch. f. path. Anat. **116**:85, 1889.

27. Gwynne, C. N.: Two Cases of Multiple Xanthoma Tuberosum, Rep. Soc. Study Dis. Child. **5**:318, 1905.

28. Hess, F. O.: Ueber allgemeine Xanthomatose, Verhandl. d. deutsch. Gesellsch. f. inn. Med. **46**:355, 1934.

xanthoma. In the case of xanthoma tuberosum reported by Weidman and Boston [29] postmortem examination also revealed involvement of the heart and aorta.

It was suggested by Chalatow [30] and Weber [31] to examine near relatives of patients with xanthoma for hypercholesteremia or other infiltrations of cholesterol related to xanthoma, such as arteriosclerosis, arcus senilis or gallstones. The value of these suggestions has been confirmed by numerous reports. In the family reported on by Lapowski, for instance, 2 sisters showed mitral disease and enlargement of the liver in addition to hypercholesteremia and xanthoma, while a brother and the mother had only hypercholesteremia. In the family reported on by Lane and Goodman, the father and a daughter had hypercholesteremia, xanthoma tuberosum and heart disease, whereas in another daughter only hypercholesteremia was found.

In recent years the association of cutaneous xanthoma with angina pectoris has been emphasized by Müller [32] and Svendsen.[33] It is not surprising, therefore, that in 65 cases of xanthoma tuberosum Montgomery observed that in 40 per cent there was angina pectoris, coronary sclerosis or occlusive vascular disease of the extremities producing intermittent claudication.

CLINICAL OBSERVATIONS OF THE B. FAMILY

The Pennsylvanian family studied by us was of Syrian descent. The parents were second cousins once removed and had 13 children (fig. 1). Four of these children may be excluded from our survey, since 1 of them was still an infant and 3 had died at, or shortly after, birth. In 5 of the 9 remaining children xanthoma tuberosum developed, and 4 of these 5 died more or less suddenly.

It was possible to obtain cholesterol analyses for practically all members of this family, including most of the half-siblings of the mother. For 3 of the deceased children the blood cholesterol was determined at the Wilkes-Barre General Hospital according to a modified method of Bloor, with the upper limit

29. Weidman, F. D., and Boston, L. N.: Generalized Xanthoma Tuberosum with Xanthomatous Changes in Fresh Scars of an Intercurrent Zoster: Adenocarcinoma of the Ampulla of Vater at Necropsy, Arch. Int. Med. **59**:793 (May) 1937.

30. Chalatow, S. S.: Die anisotrope Verfettung im Lichte der Pathologie des Stoffwechsels (Die Cholesterindiathese), Jena, Gustav Fischer, 1922.

31. Weber, P. F.: Cutaneous Xanthoma and "Xanthomatosis" of Other Parts of the Body—Pituitary Xanthomatosis—"Xanthomyelomata" of Tendon-Sheaths, etc., and the "Cholesterin Diathesis," Brit. J. Dermat. **36**:335 (Aug.-Sept.) 1924.

32. Müller, C.: Xanthomata, Hypercholesteremia, Angina Pectoris, Acta med. Scandinav., 1938, supp. 89, p. 75; Angina Pectoris in Hereditary Xanthomatosis, Arch. Int. Med. **64**:675 (Oct.) 1939.

33. Svendsen, M.: Are Supernormal Cholesterol Values in Serum Caused by a Dominantly Inherited Factor? Report of a Family Investigation of Thirty-Four Individuals, Acta med. Scandinav. **104**:235, 1940.

determined at 220 mg. per hundred cubic centimeters of serum. For the patients whom we could study personally, additional examinations were made at the New York Post-Graduate Medical School and Hospital. The methods employed here were those of Sackett [34] for total cholesterol, of Bloor [35] for total lipids and of Whitehorn [36] for lipid phosphorus. According to these methods. the normal range is considered to be 500 to 700 mg. per hundred cubic centimeters for total lipids, 7 to 14 mg. for lipid phosphorus, and 160 to 230 mg. for total cholesterol.

The father of the tainted siblings (fig. 1 : I, 1) had been born in Syria and was 51 years old. While the information about his ancestors was incomplete, we know that his own history up to the age of 37 was irrelevant. After that he suffered from attacks of indigestion and intolerance for food, due to a chronic infection of the gallbladder. This condition was considered the cause of some substernal pain radiating to the shoulders and arms, of which he had been complaining for the past three years. Physical and electrocardiographic examination of the heart revealed no evidence of cardiovascular disease, except for hardening of the palpable arteries. Although there were no changes in the skin or viscera,

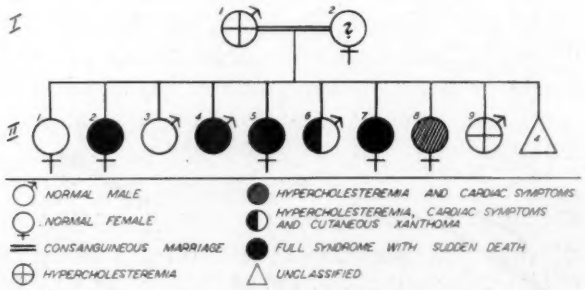

Fig. 1.—Descent table of the B. family showing inheritance of xanthomatosis.

the cholesterol content of the serum was found to be increased, as the following figures indicate:

	Mg. per 100 Cc.
Total lipids	893.3
Fatty acids	578
Lipid phosphorus	9.6
Cholesterol	315

The mother (fig. 1 : I, 2), aged 40, was a maternal second cousin to her husband. She also had been born in Syria and had only 2 siblings, in addition to 2 half-brothers and 6 half-sisters, the offspring of her mother from a second marriage. One sibling died at birth and the other at the age of 20 months, of unknown cause, while her mother died at the age of 48 of heart trouble and the father at the age of 50 of unknown cause. She herself married at the age of 13 and had 13 children, of which 2 died at birth and 1 in infancy, of unknown cause. Her past history was irrelevant, and physical examination revealed no

34. Sackett, G. E.: Modification of Bloor's Method for the Determination of Cholesterol in Wholè Blood or Blood Serum, J. Biol. Chem. **64**:203 (May) 1925.

35. Bloor, B. R.: The Determination of Small Amounts of Lipid in Blood Plasma, J. Biol. Chem. **77**:53 (April) 1928.

36. Whitehorn, J. C.: A Method for the Determination of Lipoid Phosphorus in Blood or Plasma, J. Biol. Chem. **62**:133 (Nov.) 1924.

abnormalities other than varicosities of the legs. Examination of the blood showed a normal content of total lipids, fatty acids, lipid phosphorus and cholesterol, while in 5 of 7 half-siblings examined marked hypercholesteremia was noted.

Of the children, the oldest daughter (fig. 1: II,1), aged 26, had always been well. Physical examination of the skin and internal organs showed no abnormalities except an accentuated second pulmonic sound. Examination of the blood revealed a normal content of cholesterol and lipid phosphorus, a slight increase in total lipids and a marked increase in fatty acids. However, the last observation may be disregarded because the blood was not taken after a fasting period.

The second child (fig. 1: II, 2) died suddenly in October 1939 at the age of 23. She had been in good health until the age of 3 years, when she had diphtheria, from which she recovered quickly. Three months later small orange-yellow nodules appeared on the skin over the achilles tendons, followed by similar lesions on the elbows, ankles, knees, hands, feet and buttocks. The nodules

Fig. 2 (fig. 1: II, 2).—Xanthoma nodes in the second child (post mortem).

became gradually larger, some of them reaching the size of a large lemon. The nodes were at times extremely painful. In 1925 several nodes were removed, and some of them were found closely connected with the tendons or with their sheaths. After the removal of the lesions new ones reappeared at the same locations and grew to the previous size.

At the age of 4 years the girl had an attack of uncomplicated pneumonia, and in 1935 she had bilateral pneumonia with pleural effusion, for which she was confined to bed for a few months. Apart from these illnesses she had no particular complaints until her admission in 1939 to the Wilkes-Barre General Hospital, where she was treated for an abrasion of the skin of the left knee over one of the tumors. According to the record, there were multiple tumors of soft and firm consistency, ranging from the size of a pea to that of a lemon and located on the fingers, wrists, elbows, shoulders, breasts, toes, ankles, knees and hips (fig. 2). The nodes were attached to the skin or to the underlying tissues and had a smooth or nodular surface. Since the ulceration on the knee resisted treatment and the patient's activities were hindered by the multiple growths,

numerous nodes were removed from the heels, knees and buttocks, varying in size from 4 to 12 cm. in diameter.

Microscopic examinations of the nodes confirmed the clinical diagnosis of xanthoma. According to the pathologic reports, which included one by Dr. David

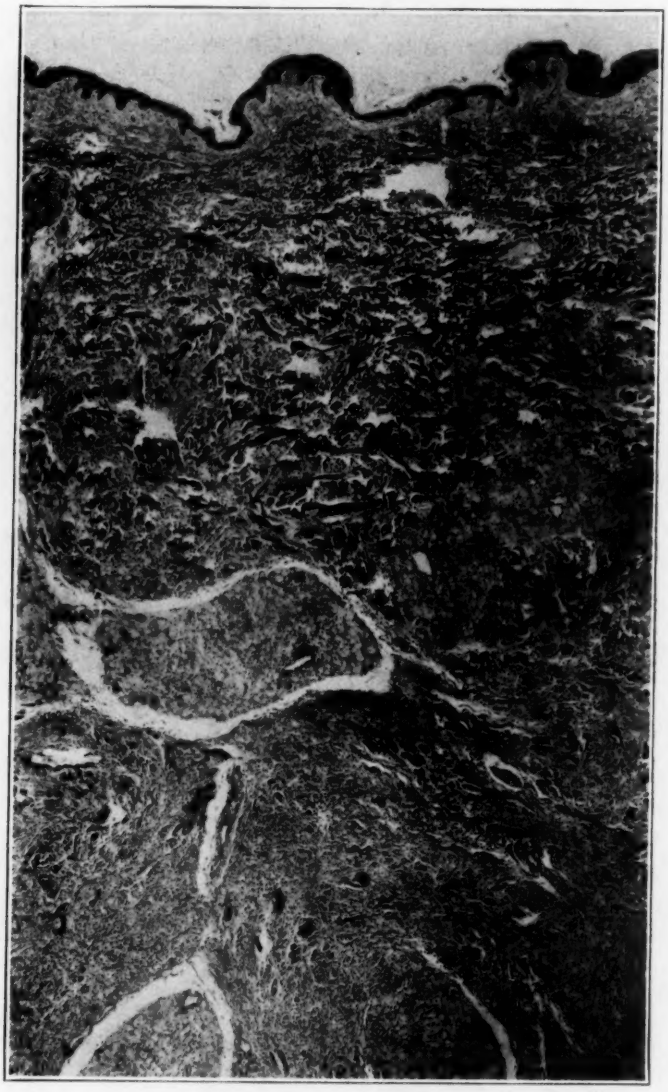

Fig. 3.—Xanthomatous infiltrations in the cutis.

Satenstein, small scattered foci of cell infiltrates extended from the upper part of the cutis down to the middle and deep parts of the cutis, where they expanded into large islands. There was no inflammatory reaction. The infiltrates were composed of characteristic foam cells of various shapes, as seen in xanthoma. The changes in the cell bodies were fairly uniform. The spongioplasm was

visible as a fine network, and the cytoplasm was apparently absent, taking no stain. There were also a few multinucleated cells (figs. 3 and 4).

Examination of the heart revealed a blowing systolic murmur at the apex as the only abnormality. There was no enlargement of the spleen or liver. Labora-

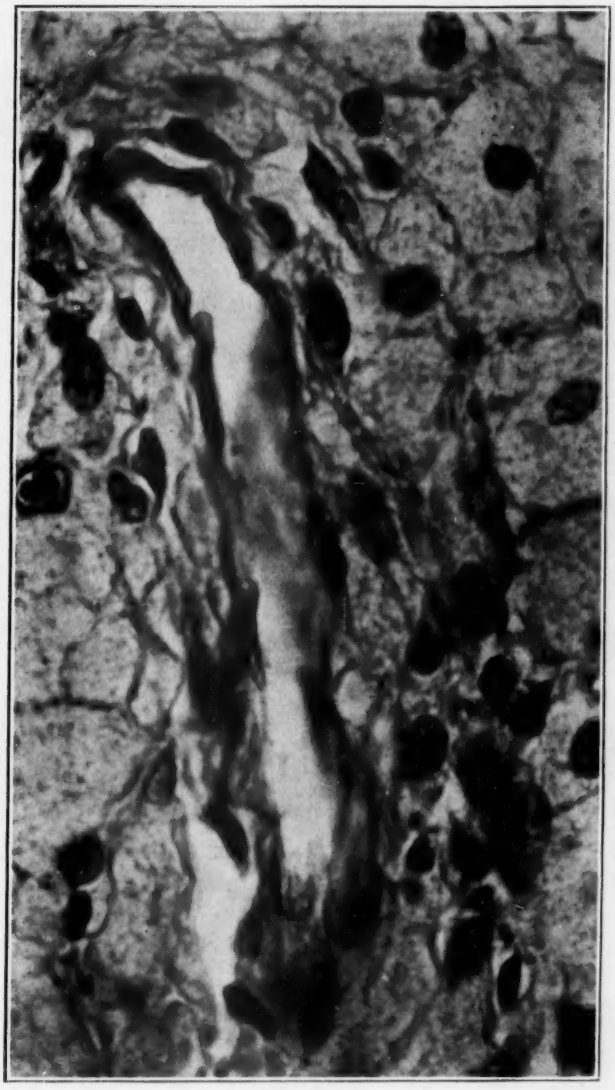

Fig. 4.—Foam cells in xanthoma node (high power).

tory examinations showed a normal blood and differential count, normal urine and negative Wassermann and Kahn reactions of the blood. The cholesterol content of the blood was increased to 266 mg. per hundred cubic centimeters.

The patient was discharged from the hospital in June 1939, apparently in satisfactory health. On the evening of Oct. 10, 1939, after a day during which

she had felt perfectly well, she walked to church, a distance of about 1½ miles (2,415 meters), one third of the way uphill. About fifteen minutes after entering church she suddenly slumped over without making any outcry and died. Postmortem examination was performed and revealed interesting changes, which will be discussed in another part of the paper.

The third child (fig. 1: II, 3), a youth aged 20, had always been in good health. Periodic examinations since his childhood failed to reveal any cutaneous or visceral abnormalities. The cholesterol content of his blood was not determined.

The fourth child (fig. 1: II, 4) died in 1940, at the age of 18. This boy had always been in good general health, except for having measles and diphtheria in early childhood and xanthoma tuberosum, which had appeared at the age of 3½

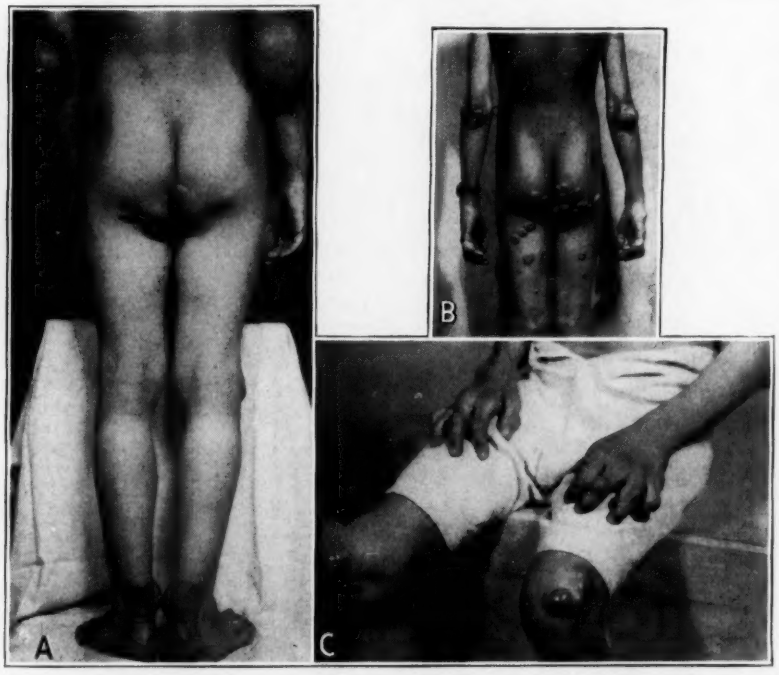

Fig. 5 (fig. 1: II,4).—*A,* large xanthoma tumors in the fourth child. *B* (fig. 1: II,5), xanthomatous nodes and plaques in the fifth child. *C* (fig. 1: II,6), xanthoma nodes in the sixth child.

years. The eruption resembled that of the other siblings (fig. 5 *A*). In 1938 the parents were told by the family physician that the boy had heart disease, although he had never complained of any symptoms. In July 1939 several nodes were removed, and the diagnosis of xanthoma was confirmed by microscopic studies. The record of the examination of the heart at that time showed an acceleration to 100 beats per minute, a soft systolic murmur at the apex and an accentuated second aortic sound. Laboratory examinations of the blood and urine showed no abnormalities except the cholesterol content of the blood, which was increased to 285 mg. per hundred cubic centimeters.

On the morning of July 30, 1940 the boy began to complain of weakness. He perspired profusely, was pale and cold, made several attempts to vomit and tossed

about in bed as if in pain. Other members of the family had complained of similar symptoms, from which they had soon recovered. The boy, however, became progressively worse, and in spite of stimulating treatment he died within two and one-half hours. The illness of all the members of the family was diagnosed as accidental poisoning, which was also considered to be the cause of death of this boy. However, in view of the sudden death of the other siblings, it seemed justified to attribute this fatality to xanthomatous involvement of the cardiovascular system.

The fifth child (fig. 1: II, 5), a girl, died in 1940, at the age of 14. At the age of 3 years xanthoma tuberosum developed, which resembled the eruption described in the other affected siblings (fig. 5 *B*). When she was 6 years old the family physician made a diagnosis of heart disease. Although the child was frail and did not grow at a normal rate, she never complained of any discomfort and attended school regularly. At the age of 8 years she had an attack of difficult breathing, associated with swelling of the abdomen, belching and prostration. Since she made a rapid recovery, it was not realized then that the sudden illness might have been due to some acute cardiac condition.

The results of laboratory examinations in 1937 were normal except for an increased cholesterol content of the serum, amounting to 333 mg. per hundred cubic centimeters.

On Jan. 20, 1940 the girl went to bed feeling perfectly well. In the middle of the night she awoke and complained of slight pain in the sternal region. She fell asleep again and slept till morning. Although she then still complained of pain, she did not appear to be in a worse condition than she had been the night before. Shortly afterward, however, she was found dead by her mother, who had left her alone for only fifteen minutes.

The sixth child (fig. 1: II,6), a boy aged 11½ years, was the only surviving child with xanthoma tuberosum. At the age of 3 years he had an attack of acute hemorrhagic nephritis, followed by appearance of the eruption six months later.

Our examination showed lesions of xanthoma similar to those in the other affected siblings (fig. 5 *C*). In addition, there were xanthelasma-like plaques in several of the finger webs, over some of the nodes and in their vicinity. The boy had no physical complaints although auscultation of the heart revealed a diastolic murmur at the apex and the electrocardiogram showed sinus tachycardia. The cholesterol content of the blood, which in 1935 had amounted to 400 mg. per hundred cubic centimeters, was found in 1941 to be still more increased, as indicated by the following figures:

	Mg. per 100 Cc.
Total lipids	1,696
Fatty acids	956
Lipid phosphorus	17.1
Cholesterol	730

The seventh child (fig. 1: II, 7), a girl, died in 1938, at the age of 6½ years. She apparently was in good health and was never attended by a physician. Lesions of xanthoma tuberosum were noticed by her family when she was 4 years old. Although the nodes became large, the child did not seem to be handicapped.

On the evening of Feb. 29, 1938 the girl retired, seemingly in good health. However, she soon awoke, complaining of severe pain in the epigastrium and around the umbilicus. About one hour later she was found by the summoned physician in a convulsive seizure, expelling frothy sputum from the nose and mouth. She died fifteen minutes later.

Although no record of the physical status or of the blood chemistry is available in this case, the association of xanthoma tuberosum and sudden death indicates a similar cardiovascular damage as in the other deceased siblings.

The eighth child (fig. 1: II,8), a girl aged 8 years, had a history of probable chorea minor at the age of 4 years and of repeated attacks of epistaxis at the ages

Fig. 6 (fig. 1: II,2).—Extensive lipoid involvement of the descending and abdominal aorta.

of 4 and 5 years. In 1938 examination of the heart revealed an organic lesion, which was confirmed by an electrocardiogram and a roentgenogram. Our examination showed no evidence of cutaneous involvement, but there was a systolic murmur at the apex of the heart with an accelerated rate, 92 beats, and an increase in the cholesterol content of the blood, to 280 mg. per hundred cubic centimeters.

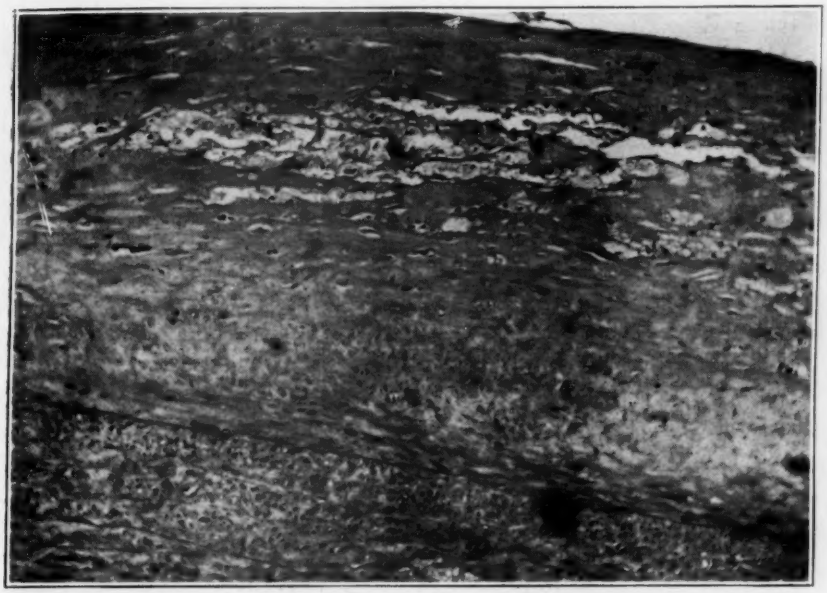

Fig. 7.—Typical lipoid deposit in the intima of the aorta (low power).

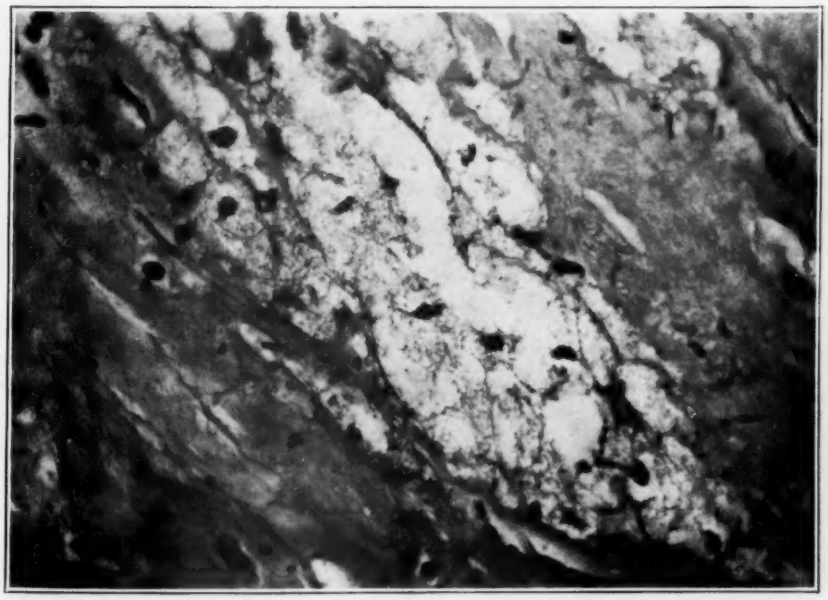

Fig. 8.—Foam cells in a lipoid deposit (high power).

The ninth child (fig. 1: II,9) was a boy aged 4½ years whose history was irrelevant. Physical examination failed to show any cutaneous or visceral changes except an increased rate of the heart beats, a slightly shortened duration of the heart sounds and again a definite increase in the cholesterol content of the blood, as shown by the following figures:

	Mg. per 100 Cc.
Total lipids	825
Fatty acids	462
Lipid phosphorus	2.9
Cholesterol	355

NECROPSY OBSERVATIONS IN THE CASE OF THE SECOND CHILD (FIG. 1: II, 2)

In the case of the second child, who died suddenly at the age of 23, we were fortunate enough to obtain a comprehensive report on the autopsy, which was performed by Dr. W. L. Lanyon, of the Wilkes-Barre General Hospital. The most significant visceral changes were those of the cardiovascular system, and coronary sclerosis was assumed to be the immediate cause of death. The heart showed myocardial degeneration in addition to marked coronary sclerosis. Throughout the entire length of the aorta there were scattered orange-yellow lipoid deposits, giving the appearance of very advanced arteriosclerosis. Similar lipoid deposits were found in all the arteries of the body, including the renal arteries, and in the pyramids of the kidneys.

Other observations were as follows: chronic pleuritis; perisplenitis; perihepatitis; moderate parenchymatous degeneration of the liver, spleen and pancreas; bilateral basal congestion of the lungs; acute passive congestion of the spleen; bilateral nephrosis; mesenteric adenopathy, and depletion and medullary degeneration of the adrenal glands.

Dr. Lanyon made available to us the descending and abdominal aorta (fig. 6), which was reexamined by Dr. Arthur Ginzler, of the Sydenham Hospital. According to his report, the aorta was moderately elastic. The major portion of the intimal surface was occupied by numerous irregular, slightly raised, grayish yellow and yellow plaques, giving the appearance of advanced atheromatosis. Microscopically, the intima was thickened in places by hyalinized fibrous plaques which contained collections of large macrophages, appearing as typical foam or xanthoma cells (figs. 7 and 8). Frozen sections stained with sudan IV showed that these cells contained abundant lipid.

COMMENT

In summarizing our observations on the B. family, we may repeat that the mother of the tainted siblings was free of any abnormality of the skin, viscera or blood, while the father had only hypercholesteremia in addition to a chronic form of cholecystitis. Of the 9 children included in our analysis, 5 had xanthoma tuberosum, which had developed before the age of 4 years. Four of these 5 died more or less suddenly at the ages of 6½, 14, 18 and 23 years, respectively. In 1 of the deceased patients necropsy revealed extensive involvement of the heart, aorta and other arteries and also some lipoid deposits in the kidneys and renal arteries. Cardiac defect and hypercholesteremia had been diagnosed in 3 of the deceased children during their life time, but no record of the condition of the heart or of the blood chemistry was available for the fourth child. In view of the fact, however, that this girl not only had xanthoma tuberosum but also died suddenly at the age of 6½ years, we

are inclined to assume that she was afflicted with hypercholesteremia and cardiovascular disease in the same way as the other deceased children.

In addition to the 1 surviving boy who exhibits the syndrome of xanthoma tuberosum, cardiac defect and hypercholesteremia, there are 4 other living children without cutaneous xanthoma. Of these 4, an 8 year old girl has heart disease and hypercholesteremia, while a boy aged 4½ years has hypercholesteremia without involvement of the skin or any definite disorder of the heart. The 2 remaining children have remained free of any abnormality, so far as we have been able to determine.

It may also be recalled that the parents of these strongly tainted siblings had no cutaneous or cardiovascular symptoms, although the father had hypercholesteremia and was a cousin of his wife, whose half-siblings were also hypercholesteremic. This observation appears to be in support of the theory that hypercholesteremia rather than xanthoma tuberosum is the principal manifestation of a directly inherited factor for a special form of disturbance of lipoid metabolism leading under certain conditions to cutaneous as well as to cardiovascular changes.

Regardless of whether xanthoma tuberosum is an ordinary expression of the original factor for the disturbance of lipoid metabolism or requires the assumption of an additional genetic mechanism to explain the specific susceptibility of the skin, it is evident that the accumulation of morbid factors in the present family is excessive for both hypercholesteremia and the secondary changes in the skin and blood vessels. The proportions of affected and unaffected children amount to 77 and 23 per cent respectively, and the distribution of this taint does not correspond to any of the usual ratios found in the simple modes of recessiveness or dominance. In case of single dominant inheritance, only 50 per cent of the children should be affected, if it is assumed that the father alone is heterozygous for the anomaly and the mother is classified as normal. The same 1 : 1 ratio of affected to unaffected children should be expected in simple recessiveness, if the father is classified as homozygous and the mother—being a second cousin to her husband and the half-sister of a tainted subject—as heterozygous. On the other hand, if both parents are assumed to be heterozygous for a recessive trait, a still smaller proportion of affected children (1 : 3) would be the average expectation.

Even if the possibility were disregarded that the unusually high incidence of taint, 77 per cent, might be due either to chance or to the elimination of the 4 children not included in the account, it would not be impossible to give another genetic explanation for this accumulation of trait carriers in the B. family. For instance, in accepting the theory of simple dominance, one would expect a theoretic incidence of 75 per cent, if the father could be classified as homozygous for hypercholesteremia

and the mother as a heterozygote with inhibited manifestations of the taint. Another possible explanation would be that the given genotype in the B. family was recessive and expressible only to about 75 per cent. In this case it would be feasible to assume that both parents were homozygous for a recessive factor which was manifested only by the father in the form of hypercholesteremia.

Since practically all of these assumptions would require one to presuppose that hypercholesteremia and xanthoma tuberosum originate from the same genotype and represent merely different clinical symptoms of a common basic disturbance in lipoid metabolism, it seems essential to emphasize that no adequate statistical data are as yet available to substantiate this supposition conclusively. It is true that the frequency of hypercholesteremia has been found to be increased in blood relatives of persons affected by xanthoma tuberosum. However, no studies have so far been carried out to show a correspondingly consistent increase of both hypercholesteremia and xanthoma tuberosum among the blood relatives of persons affected by hypercholesteremia only.

It is appropriate to conclude, therefore, that the analysis of the taint distribution in the B. family is not in discord with the current genetic concept of xanthomatosis. According to this theory, xanthoma tuberosum is to be considered as a special form of essential xanthomatosis, which is based on a specific, autosomal and apparently dominant genetic factor, probably in close connection with a constitutional deficiency in lipoid metabolism. However, present data do not yet permit one to draw any definite inferences about the various genetic mechanisms which seem to operate in the transmission and manifestation of the trait.

The urgency of the task to clarify the complex genetic problems involved in the pathogenesis of this type of lipoid metabolism disturbance needs no particular emphasis. No satisfactory progress in systematic treatment and prevention of xanthoma tuberosum can be expected without complete knowledge of the heredoconstitutional mechanisms by which this anomaly is transmitted and manifested.

When one considers the close etiologic relations between xanthoma tuberosum and hypercholesteremia, it seems advisable at present to concentrate therapeutic as well as preventive efforts for this disease on the disturbance of the cholesterol content of the blood. In accordance with the studies of Gaál,[37] Schönheimer,[38] Huber, Broun and Casey [39]

37. Gaál, A. M.: Untersuchungen über Cholesterinstoffwechsel bei Xanthomatosis essentialis, Ztschr. f. klin. Med. **113**:349, 1930.

38. Schönheimer, R.: Ueber eine Störung der Cholesterin-Ausscheidung, Ztschr. f. klin. Med. **123**:749, 1933.

39. Huber, M. J.; Broun, G. O., and Casey, A. E.: Prevention of Arteriosclerosis in the Rabbit by Use of Pancreatic Extract (Lipocaic), Proc. Soc. Exper. Biol. & Med. **37**:41 (Dec.) 1937.

and other investigators, it may be possible by the institution of a regimen, including a strict cholesterol-free and fat-free diet or by the administration of a pancreatic extract in such cases of generalized xanthomatosis (including xanthoma tuberosum, angina pectoris and occlusive vascular disease of the extremities) to reduce hypercholesteremia and thus possibly control the tendency to cutaneous and vascular complications.

SUMMARY

Familial incidence of xanthoma tuberosum has been observed in a Syrian family which in addition to the unaffected but consanguineous parents and 4 unclassified infants consists of 9 children and 8 half-siblings of the mother. Of the 5 children in whom xanthoma tuberosum developed before the age of 4 years, all were affected by a generalized disturbance of the lipoid metabolism (hypercholesteremia), and 4 died suddenly between the ages of 6 and 23 years, the cause of death being attributable to xanthomatous lesions in the cardiovascular system.

The observation of hypercholesteremia without cutaneous involvement in 2 additional children, in the father of the tainted siblings and in 5 of the mother's half-siblings is in support of the theory that hypercholesteremia rather than xanthoma tuberosum is the principal manifestation of the original hereditary factor. This hereditary factor seems to produce a special form of disturbance of lipoid metabolism and, under certain conditions, a more generalized syndrome of cutaneous and cardiovascular lesions as well.

Although the hereditary cause of this type of primary essential xanthomatosis has been demonstrated beyond a question, no adequate statistical data are as yet available to warrant a final analysis of the genetic mechanisms involved. The taint distribution in the B. family is not in disagreement with the present theory of dominant inheritance, but it would also be explainable by the assumption of simple recessiveness.

Careful genetic studies of families affected either by xanthoma tuberosum or by hypercholesteremia are essential for the development of successful measures of therapy and prevention.

A cholesterol-free and fat-free diet may be helpful in protecting hypercholesteremic trait carriers against the development of cutaneous and cardiovascular lesions.

Excellent cooperation was received throughout this study from the staffs of the Wilkes-Barre General Hospital and the New York Post-Graduate Hospital. Dr. Maurice Bruger made the cholesterol determinations on the blood. Dr. Arthur Ginzler made the pathologic reexamination of the viscera. Dr. Franz J. Kallmann, of the New York State Psychiatric Institute, assisted in the analysis of the genetic aspects of the family studied.

ABSTRACT OF DISCUSSION

DR. THEODORE CORNBLEET, Chicago: Anitschkow produced atherosclerosis in rabbits by feeding them cholesterol. This gave impetus to the conception of the humoral origin of xanthomatosis. Xanthomatosis has been considered a disease of the reticuloendothelial system. This arises from the fact that the foam cells in xanthoma lesions can be shown to be fixed phagocytes. The idea is that these cells simply imbibe the lipoids. This explanation leaves out of consideration whether these cells have the capacity to manufacture these lipoids de novo. It has been shown recently that under certain circumstances the neuroglia of the brain can elaborate certain lipoids. This overcomes to an extent the objection that the few xanthoma cells in several nodules could not produce all the cholesterol and other lipoids found in some patients at high blood levels. If the entire reticuloendothelial system, of which a large part is in the liver, were to produce lipoids in increased quantity and give them up, there would be no difficulty in conceiving of it as the possible source of the high blood values. Such a conception would require that the essential disorder of the reticuloendothelial cells in xanthomas is their inability to discharge their fabricated and stored lipoids. This would help to harmonize with events in disseminated xanthomatosis, in which blood lipoids are normal in quantity. Here, little of the entire reticuloendothelial system would be involved producing lipoids. When blood lipoids are high, on the other hand, it would mean that more of the reticuloendothelial system was engaged in producing the larger quantities.

Dermatologists were the first to recognize sarcoidosis of the skin, and largely through their efforts an understanding of the systemic nature of this syndrome has been established. In the same way the ease with which dermatologists may recognize xanthomatosis of the skin gives them the opportunity and task to help one understand its essential systemic character and interrelations.

DR. DAVID BLOOM, New York: The approach to this problem from the genetic point of view holds promise of aid in the clarification of this difficult subject. I agree with Dr. Cornbleet about the necessity of a complete examination of each member of such families. In the examination of our family members, data are lacking which are needed for a complete knowledge of their physical status, such as basal metabolism and results of sugar tolerance tests. These additional examinations could not be carried out owing to unavoidable circumstances. The main purpose of this paper is to stress the necessity of further genetic investigations of xanthomatosis. Family studies should be carried out starting, first, with patients affected with xanthoma tuberosum, secondly, with patients showing hypercholesteremia only and, thirdly, with the general population, obtaining reliable figures on the incidence of xanthoma tuberosum on the one hand and hypercholesteremia on the other hand; the figures obtained in these three separate investigations should be compared with each other.

CHROMOBLASTOMYCOSIS IN CUBA

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Weidman and Rosenthal [1] recently made a complete review of the literature on chromoblastomycosis and presented a new case from Pennsylvania, calling attention to the more frequent occurrence of the disease in the United States and neighboring countries.

The object of this paper is to discuss the clinical features of chromoblastomycosis, to report on 31 cases we observed in Cuba and to make some remarks on the treatment of this condition. Only brief mention will be made of our mycologic studies, as well as of the pathologic changes, since these two fields have been thoroughly covered by previous writers.

Chromoblastomycosis is not uncommon in Cuba. It is the only form of the so-called blastomycosis that we have identified, since the Gilchrist type, the Busse-Buschke type, torulosis and coccidioidal granuloma have never been observed on this island. The disease is almost exclusively one of the rural districts, and practically all patients with the condition seen in the cities are from farms and sugar plantations. Classified by us for many years under the common designation of blastomycosis, it has been recognized in Cuba as a different entity since 1936, after the publications of Emmons and Carrión [2] and Carrión.[3] Most Cuban dermatologists still consider cases of this condition to be instances

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Read at the Sixty-Fourth Annual Meeting of the American Dermatological Association, Inc., New Orleans, April 7, 1941.

From the Department of Dermatology and Syphilology, University of Habana, Medical School, service of Dr. V. Pardo-Castello.

1. Weidman, F. D., and Rosenthal, L. H.: Chromoblastomycosis: A New and Important Blastomycosis in North America, Arch. Dermat. & Syph. **43**:62 (Jan.) 1941.

2. Emmons, C. W., and Carrión, A. L.: Hormodendrum Pedrosoi: An Etiological Agent in Chromoblastomycosis, Puerto Rico J. Pub. Health & Trop. Med. **11**:639 (June) 1936.

3. Carrión, A. L.: Chromoblastomycosis: A New Clinical Type Caused by Hormodendrum Compactum, Puerto Rico J. Pub. Health & Trop. Med. **11**:663 (June) 1936.

of Gilchrist's blastomycetic dermatitis; indeed, the clinical resemblance is close and only histologic and mycologic studies permit differentiation.

For a number of years we had diagnosed the condition in our cases by identifying the typical round yellow or chestnut brown bodies in the sections of tissue but had been unable to secure cultures and identify the causal organism until, under the advice of Dr. Fred D. Weidman, we planted small bits of tissue in Sabouraud dextrose agar. Since 1938 we have made an effort to investigate all suspected cases histologically and mycologically, with the result that a large number of instances of this disease have been collected and we have been able to prove that in many cases of verrucous, papillomatous, tuberculoid and syphiloid dermatoses the condition in reality was a clinical type of chromoblastomycosis.

CLINICAL STUDIES

We have divided the conditions in our cases into five different types: (1) verrucous, (2) tuberculoid, (3) syphiloid, (4) psoriasiform and (5) cicatricial and elephantiasic.

1. The verrucous, or papillomatous, type is the most common. It is most often encountered on the legs in the form of elevated, hypertrophic, hyperkeratotic or soft patches, sometimes in one continuous mass and other times in separate foci 2 to 3 inches (5 to 7.5 cm.) in diameter. These lesions begin as aggregated small nodules or papules with a scaly surface, but they undergo hypertrophy and form the typical sharply circumscribed masses. The color varies from light brown to dark red according to the amount of keratotic material accumulated on the surface. When hyperkeratosis is not a prominent feature the lesions are soft and red. Among the masses of newly formed tissue small collections of pus occur, which can be easily expressed, the pus being sometimes cheesy and at other times more fluid, usually white or yellowish or stained with blood. Suppuration is never a feature when the disease is uncomplicated, and when present it is due to secondary infection with pus organisms. These lesions are usually foul, owing partly to maceration and partly to secondary infection, as is always the case in papillomatous manifestations on the skin. Usually only one foot or leg is affected; we have not encountered a case in which the condition was bilateral. The dermatosis may cover a few inches of skin, but sometimes large areas are affected. In one of our cases the entire lower extremity from the dorsum of the foot to the groin was covered by a continuous mass of verrucosities. Separate small masses may have a frambesiform appearance, arising abruptly from an apparently sound skin, with little or no surrounding inflammation or even hyperemia. Occasionally areas of spontaneous cicatrization may occur among the

hypertrophic masses, and then the lesions may assume the form of a ring of verrucosities surrounding a white retracted scar.

2. The tuberculoid type resembles tuberculosis verrucosa cutis or sarcoid. The lesions are usually small circumscribed patches of brown

Fig. 1.—Chromoblastomycosis of the verrucous type, showing central scarring with ring formation (not uncommon).

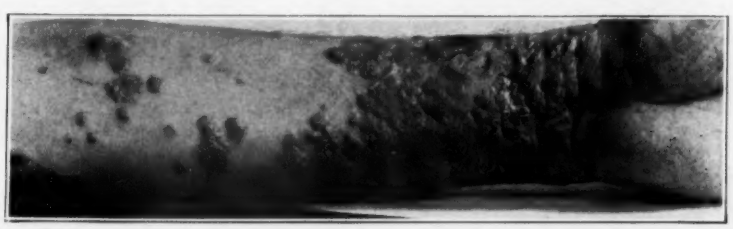

Fig. 2.—Chromoblastomycosis of the tuberculoid type. The lesions are dark red infiltrated papules resembling sarcoid; duration, two years.

hypertrophic nodules with erythematous areolas and little scaling. In 1 of our cases (fig. 2) the lesions extended from the wrist to the bend of the elbow, the color being purple, resembling lesions of sarcoid. In

most cases the differential diagnosis from tuberculosis verrucosa cutis and perhaps from sarcoid may be extremely difficult from a clinical standpoint and only histologic studies may permit differentiation. In cases of this type miliary abscesses are lacking, but typical round fungous cells may be identified in the scales scraped from the surface, when treated by sodium hydroxide and examined under the dry high power objective. This condition is often of short duration compared with the

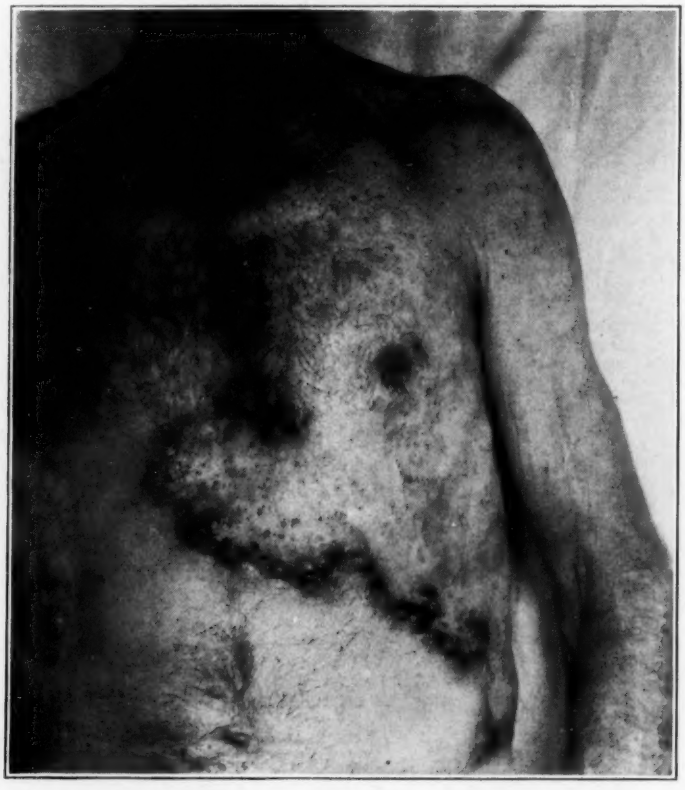

Fig. 3.—Chromoblastomycosis of the syphiloid type. Notice the extensive scarring with active serpiginous border. The condition extended to the dorsal and lumbar regions; duration, more than eighteen years.

verrucous types. For the latter most patients claim a duration of from five to thirty years, while for the tuberculoid types many patients report a duration of from six months to a few years. This has made us suspect that the tuberculoid type of chromoblastomycosis may be merely an early stage of the verrucous and papillomatous types. However, the role that the allergic response of the individual tissue may play in the development of one or the other clinical type may be the real explanation.

3. The syphiloid type is distinctive indeed. In some cases it is nodular and scaly with slight erythema, the nodules being small and flattened, as in the more superficial late syphiloderms, grouped in a serpiginous, annular or arciform pattern. As a rule there are few lesions, and sometimes they occur only in one group. In the cases of this type observed by us the lesions were situated on the hands and forearms. The condition in other cases, usually of the legs, is nodular and ulcerative, with a serpiginous outline closely resembling that of a late syphilid. These lesions seem to progress in an eccentric manner, leaving a thin,

Fig. 4.—Chromoblastomycosis of the psoriasiform type. The lesions are flat papules covered by micaceous, adherent scales.

atrophic, depigmented scar; the ulcerated border is sharply marginated and rather inflammatory. No scales or verrucosities are observed; instead, there are thick adherent crusts over the ulcerations, forcible lifting of which allows a small amount of pus to exude. The base of these ulcers may be somewhat hypertrophic owing to the formation of granulation tissue.

4. The psoriasiform type is the rarest of all. It consists of one or several patches of superficial inflammatory infiltration, covered with white, micaceous, adherent scales, which at first sight offer all the clinical characteristics of a patch of psoriasis. However, the lesions are not

symmetric, do not bleed when scraped and are usually few. Abscesses and verrucosities have not been observed in this type, but when all the scales are removed some areas show short papillary projections.

5. The cicatricial and elephantiasic types are usually found on the legs. However, in 1 case we observed the condition on the arm; in another case the lesions on the chest were frankly syphiloid, while on the back a huge atrophic scar extended from the shoulder blades to the lumbar region, with only one small patch of verrucous infiltration active at the lower end of the scar. The lesions are usually extensive, to say the least. The patients always give a history of trauma followed by the development of verrucosities, which seem to heal spontaneously, leaving either thick, irregular scars or atrophic and depigmented ones. Here and there on such lesions scaling and verrucous spots may be observed and at times small ulcerations and abscesses. When the leg is affected

Fig. 5.—Chromoblastomycosis of the cicatricial and elephantiasic type. Spontaneous healing in the course of years resulted in almost complete disappearance of the verrucous lesions. Only a few isolated spots are visible on the dorsa of the foot and toes.

it appears elephantiasic, and some places, especially about the foot, may have the appearance of the so-called "mossy foot" due to the accumulation of short dark vegetations and dark, dirty, keratotic material. This may be the end stage of some of the verrucous types in which an altered capacity to react results in a tendency toward the formation of fibrous tissue. We believe that elephantiasic enlargement is due to interference with the lymphatic circulation, these patients suffering often from attacks of recurring lymphangitis.

REPORT OF CASES

Of the 31 cases collected by us, 20 were encountered in Habana and 11 in Santa Clara. All the patients except 1 were farmers who came to the city hospitals for diagnosis and treatment. All were males, and

all but 4 were white. In 17 cases the lesions were situated on the lower extremities, in 5 cases on the hand, in 6 cases on the hand and forearm, in 1 case on the back and chest, in 1 case on the shoulder near the posterior axillary fold and in 1 case on the right buttock. The right and left sides were affected in about equal proportion. The palms and soles were free in practically all cases. The youngest patient was 14 and the oldest 70, but the majority were between 40 and 60.

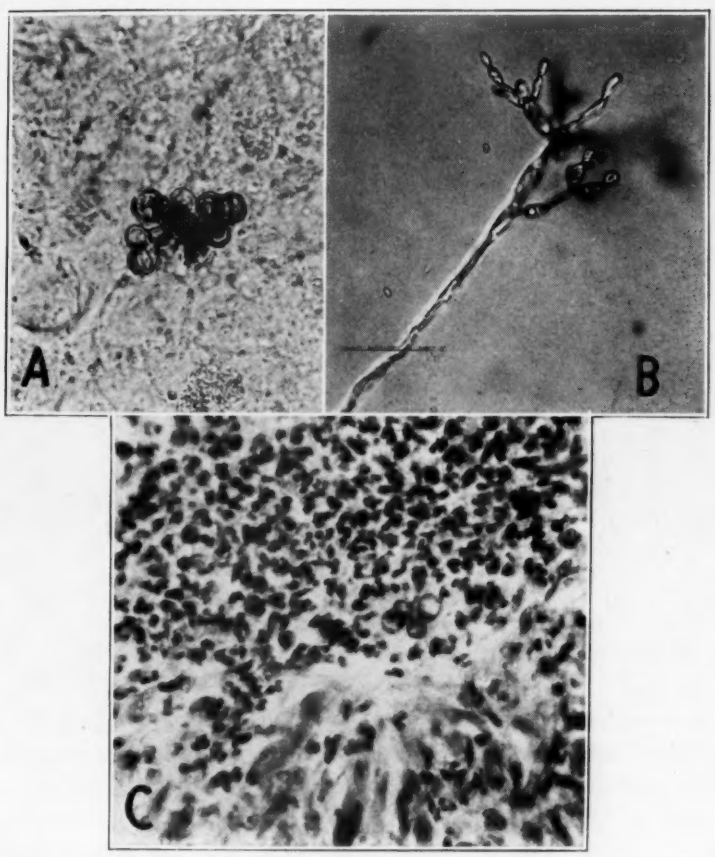

Fig. 6.—*A*, group of chestnut-colored cells in the scales. *B*, typical conidia. *C*, section of tissue showing group of 4 cells in a miliary abscess.

There were 15 cases of the papillomatous and verrucous type, 4 of the syphiloid, 4 of the tuberculoid, 4 of the psoriasiform and 4 of the cicatricial and elephantiasic type.

In all cases there was a history of trauma during the course of work, usually from a thorn, splinter or a farm implement. Secondary infection with formation of pus was common in the verrucous types, and abscess

formation with subsequent ulceration was fairly common. However, in our opinion abscesses and ulcers are secondary manifestations and do not form a part of the uncomplicated clinical picture. Microscopic abscesses are often seen in the pathologic sections but never grow to macroscopic proportions unless pyogenic infection occurs. In some cases chronic enlargement of the lymphatic glands was observed, most likely due to secondary infection, but we have never seen a suppurating gland. Itching was absent in practically all cases, except in those of the psoriasiform type.

Thirty-One Cases of Chromoblastomycosis

Sex	Race	Age	Location	Clinical Type	Duration
M	W	46	Left foot	Papillomatous	4 years
M	W	49	Dorsum of hand	Papillomatous	5 years
M	W	54	Left elbow	Psoriasiform	.....
M	W	42	Hand and forearm	Syphiloid	20 years
M	W	55	Left foot	Papillomatous	4 years
M	C	47	Right leg and thigh	Papillomatous	20 years
M	W	59	Dorsum of foot	Papillomatous	.....
M	W	59	Right forearm	Papillomatous	5 years
M	W	49	Forearm	Syphiloid	5 years
M	W	29	Left foot	Papillomatous	1 year
M	W	54	Right leg	Papillomatous	19 years
M	W	54	Left leg and foot	Papillomatous	3 years
M	W	51	Right leg	Cicatricial	18 months
M	W	55	Hand and forearm	Cicatricial	15 years
M	C	40	Foot	Papillomatous	9 years
M	W	58	Foot and leg	Cicatricial	.....
M	W	32	Foot and leg	Papillomatous	2 years
M	W	65	Leg	Papillomatous	20 years
M	C	14	Right knee	Tuberculoid	6 months
M	W	53	Chest and dorsum	Syphiloid	18 years
M	W	48	Left hand and forearm	Tuberculoid	2 years
M	W	68	Right hand and forearm	Cicatricial	25 years
M	W	51	Left leg	Papillomatous	14 years
M	W	55	Left leg and thigh	Tuberculoid	20 years
M	W	70	Right buttock	Psoriasiform	7 years
M	W	60	Right wrist	Psoriasiform	6 years
M	W	54	Right hand	Papillomatous	7 years
M	W	38	Base of index finger	Psoriasiform	4 years
M	W	38	Left leg	Syphiloid	9 years
M	C	40	Right shoulder	Tuberculoid	3 years
M	W	60	Dorsum of right foot	Papillomatous	5 years

In our patients the disease remained limited to the skin and never affected the bones or other subjacent structures. Atrophy of the muscles, ankylosis and osteoporosis are common on the extremities in cases of long duration, due to immobility of the parts, to scarring and to lack of use. Even in cases of the elephantiasic type the bones were not affected by the disease.

The disease seems to progress by continuity, peripheral extension or autoinoculation. In instances of autoinoculation the condition takes the form of small multiple foci. Metastasis did not occur in our cases, by way of either the lymphatics or the blood stream. No visceral lesions were observed and no systemic symptoms recorded, except in a few cases in which lymphangitis due to streptococcic infection was superimposed on the parasitic disease. However, one of us (E. R. L.) has observed 2 cases in which acute febrile outbreaks were followed by the

appearance of new verrucous lesions. Treatment with potassium iodide seemed to control these febrile attacks and prevent their recurrence. The general health of the patients remained unimpaired, even in cases of twenty and more years' duration. In no case were there any changes in the blood count, except those changes attributable to the presence of intestinal parasites, with which most of our patients were infested. In 2 cases there was a coincident history of syphilis with positive serologic reactions.

DIFFERENTIAL DIAGNOSIS

The conditions which we considered in making a differential diagnosis were: tuberculosis verrucosa cutis, pyoderma vegetans, bromoderma vegetans, tertiary syphilids, psoriasis, yaws, Gilchrist's dermatitis and sarcoid.

In 1 case the lesions of hemorrhagic sarcoma of Kaposi gave rise to considerable doubt. Leishmaniasis is unknown in Cuba and was therefore easily ruled out.

The differential diagnosis rests on the finding of the typical groups of round, yellow or chestnut-colored cells in the scales, pus and sections of tissue. In the psoriasiform and in the tuberculoid types, these organisms are easily demonstrable in sodium hydroxide preparations of the scales. They are more difficult to find in the pus, especially when secondary infection is predominant. In the sections of tissue the cells are found within giant cells, in the miliary abscesses and sometimes singly in the connective tissue or between the malpighian cells. Their presence is characteristic; no other parasitic disease presents these typical cells.

HISTOLOGIC STUDIES

The histologic picture in our cases corresponds with that reported by Weidman and others. The epidermis shows intense hyperkeratosis in the verrucous types and slight hyperkeratosis and parakeratosis in the psoriasiform types. In all types there is acanthosis, more evident in the papillomatous and verrucous types, the interpapillary processes being enormously enlarged and invading the corium deeply in a disorderly manner. In some sections there are small collections of polymorphonuclear leukocytes, suggesting miliary abscesses. In a few cases we observed a tendency to the formation of cellular monstrosities and of corneous whorls, which resembled those of epithelioma but were without evidences of true malignancy.

The corium, in all types of the condition, is the seat of a thick cellular infiltration invading the papillary layer, but most abundantly the reticular layer. This cellular infiltrate is composed of polymorphonuclear leukocytes, lymphocytes, epithelioid cells and giant cells in variable propor-

tions. Eosinophils, plasma cells and some Russell bodies may be found in some specimens, plasma cells being especially abundant in many sections around the main infiltration. In some cases miliary abscesses predominate, usually well circumscribed, while in others the aspect is frankly tuberculoid, with epithelioid cells and lymphocytes surrounding giant cells of the Langhans type. Giant cells and abscesess may coexist in the same section. In the giant cells or outside of them and in the miliary abscesses round, yellow, brown or chestnut-colored bodies may be found in groups of two, four or more, sometimes in clusters.

MYCOLOGIC STUDIES

In the sections of tissue the organisms appear as round cells, varying in diameter from 7 to 15 microns. They are usually well rounded but occasionally may be polyhedral. The color varies from light yellow in some specimens to dark brown in others. They are grouped in twos and fours and sometimes in clusters in which the number of elements is difficult to count. Some cells may appear isolated and then are usually large and have a double contour. They are observed in the giant cells, in the microabscesses and at times in the connective tissue, and occasionally one may be seen between the malpighian cells. Many of them appear divided in two by a central septum and when in clusters may give the false appearance of budding cells.

In the scales and in the pus the cells show the same characteristics but often are much larger, as much as 35 microns in diameter; the grouping and the color are similar to those seen in the sections. From many of these cells mycelium sprouts, usually light colored, septate and ramified. In the scales as well as in the sections of tissue we have observed brown amorphous granules, probably the result of the disintegration of these sclerotic cells.

Pure cultures were obtained in 11 cases. The fungus grows easily in Sabouraud's agar from plantings of the scales or small bits of tissue at room temperature. Growth begins from seven to twelve days after inoculation in the form of black dots, which spread peripherally to form round black colonies covered by an abundant duvet of lighter color or sometimes dark brown. Two of our colonies were dark green in the beginning and turned darker with age, finally becoming black. As a rule, the center presents a permanent knob, and in one of our replants from conservation medium to dextrose agar concentric ring formation was observed. The pigment does not diffuse into the medium, although the agar appears intensively black when viewed from the bottom of the tube. We have observed better growth in culture mediums with little moisture, and therefore medium that has been prepared for some time is apt to give better cultures. In a thin layer of agar in a Petri dish

the colonies grow rapidly and in about four weeks cover the surface. In old cultures (six months) the color of the duvet is mouse brown but the bottom remains jet black.

Cultures in other mediums, such as wort agar, cornmeal agar and Czapek's medium, have the features already mentioned. In conservation medium, growth is slow; the surface duvet is missing or scarce; the color is black, and the surface is heaped up, even after months. In broth the culture is intense black and floats on the surface of the medium in the form of moruloid chains, which eventually fall to the bottom, and in our experience growth is then arrested.

In microcultures growth of mycelium is observed after twenty-four hours in the form of long, regularly septate and ramified hyphae; in from five to ten days a thick mat of mycelium forms. The hyphae vary in thickness from 2 to 6 microns, and the septums are separated from 10 to 24 microns, sometimes as much as 40 microns. Frequently growth occurs in the form of chains of round elements, and then hyphal formation is scarce. Some hyphae show at the tip or laterally a row of three or four dark round cells with thick walls, from 10 to 14 microns in diameter, which closely resemble the sclerotia found in sections of tissue and in the scales and pus. These cells have been found in microcultures in a thick layer of medium and seem to develop when hyphal elements grow into the medium. Arthrospores are observed after the fourth day in all cultures and according to the medium are more or less numerous and of different size.

The organs of fructification are observed after the third day in rapidly growing strains and between seven and ten days in the slower ones. At first they appear at the extremity of fine hyphae in the form of oval spores grouped in bouquets or in the form of rosettes, and then lateral conidia also appear with similar elements. According to the medium employed and its thickness, the conidia attain full growth in from three to six days, their characteristics varying also with the thickness and nature of medium. The conidiophores may be long or short, thick or thin, septate or not, and are represented by short cellular chains, single or branched. The spores are round, oval or elliptic and from 1 to 6 microns in diameter and may be grouped in clusters of a few to several hundred. In Sabouraud's agar the conidia are usually composed of a few oval spores at the end or laterally on rather thick conidiophores. In wort agar the conidia seem to be richer and the spores longer and more closely grouped. In cornmeal agar, the conidiophores are short and thin with few branchings, and the conidia are composed of small round or oval spores so closely packed together that they appear as a mass in which the structure is difficult to recognize. In Czapek's medium branching is abundant and spores are large and

thick, sometimes disposed in chains, with elements as large as 8 microns in diameter.

The characteristics of our strains prove that all belong to the same species, the organs of fructification having the characters of Hormodendrum and Acrotheca. In one culture we were able to see phialides, but they were exceptional.

We agree with Carrión and Weidman that the fungi causing chromoblastomycosis are closely related, and it may be that all have a common origin. The existence of all three types of fructification in one of our strains supports this opinion.

TREATMENT

The classic treatment with iodides has been worthless in our experience. We have administered sodium and potassium iodide by mouth in doses as high as 10 Gm. per day, sodium iodide intravenously in doses of 1 to 2 Gm. daily and compound solution of iodine U. S. P. intravenously in doses varying from 1 to 10 cc. daily, without improvement in the great majority of cases. The local application of tincture of iodine alone or with 10 to 20 per cent salicylic acid reduces the size of the vegetations and causes a certain involution of the lesions of the more superficial types, but we have not been able to cure any patient with this treatment.

The internal administration of thymol in doses of 1 Gm. daily before breakfast was without effect. Antimony and copper in the form of different organic salts and colloidal copper intravenously also failed in our hands after prolonged trials. Sulfanilamide and its derivatives were tried in 2 cases but had no favorable effect.

Intensive roentgen ray treatment has been successful in our hands in a limited number of cases of the more superficial type of rather limited patches and has proved a useful adjuvant in other cases. The doses are from 600 to 1,200 r filtered through 1 or 2 mm. of aluminum according to the size of the vegetations.

The treatment of choice in our opinion is electrocoagulation under spinal anesthesia when the lesions are situated on the lower extremities. When the lesions are situated elsewhere we have used local anesthesia with procaine hydrochloride or general anesthesia with gas. After electrocoagulation the verrucosities are scraped off with a curet and the coagulated parts treated with a 5 per cent solution of gentian violet to prevent secondary infection. The result is a firm retracted scar after two to three months of constant care. In several cases the lesions were so extensive that treatment had to be repeated after several months because of local relapses. For the cicatricial and elephantiasic type on the lower extremities no treatment except amputation is of any avail.

SUMMARY

Thirty-one cases of chromoblastomycosis are reported and the clinical aspects discussed. The clinical types of this disease have been classified in five varieties: verrucous and papillomatous, tuberculoid, syphiloid, psoriasiform, and cicatricial and elephantiasic. These variations in the clinical picture are probably due to the more or less altered capacity to react on the part of tissues involved in the different cases and to the greater or lesser general defenses of the patient. In other words, the allergic reactivity of the affected persons give rise to the different clinical types, since in all patients the same organism has been recovered and we have found no relation between the number, situation in the tissues and species of fungi and the clinical manifestations.

The fungus recovered by us in 11 cases conforms to the descriptions of Fonsecaea pedrosoi (Acrotheca pedrosoi, Hormodendrum pedrosoi, Gomphinaria pedrosoi). It must be remarked that hormodendrum, acrotheca and phialophora forms were found in one and the same culture, making it probable that all fungi concerned in the production of chromoblastomycosis belong to close species, with the same original ancestor, as suggested by Weidman.

In making the differential diagnosis, tuberculosis verrucosa cutis, dermatitis vegetans, bromoderma vegetans, tertiary syphilids, psoriasis, yaws, Gilchrist's dermatitis and sarcoid should be ruled out. The diagnosis rests on the finding of typical yellow or brown round cells or sclerotia in the scales, pus and sections of tissue. In the latter these cells are situated within giant cells or small abscesses.

The treatment of choice is intensive roentgen therapy for the superficial types and electrocoagulation for the more extensive and infiltrated conditions.

Drs. Roberto Quero and Raul Piñeyro gave valuable assistance in preparing and studying many pathologic specimens.

ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: This is the first really worth while presentation of this subject coming from Cuba. It is true that thirteen years ago Hoffman reported a case under the heading of chromoblastomycosis, but I feel sure that the diagnosis was not established. Hoffman did not describe the microorganisms and made no statement that he saw them. He sent his tissues to Büsse in Germany, and Büsse came out later with an independent publication, which was entitled "Chromoblastomycosis"; but, singularly, with Büsse the mycologist that he was, there was no mention of the character of this fungus.

Preparatory to last year's paper on this subject with Dr. Rosenthal,[1] I wrote to Dr. Pardo-Castello, who told me that he had encountered 20 cases, and with little effort he has now run the count up to 31. It is not at all surprising that so many different clinical forms have been found in Cuba, after the experience

here in the United States and in Puerto Rico. In the presentation that Rosenthal and I made last year, wherein 7 cases were analyzed coming from the United States, there was only 1, namely, Dr. Wilson's from Fort Worth, Texas, which was of the classic verrucous type seen in Brazil. The condition in all of the others was more like tuberculosis verrucosa cutis or blastomycosis, and Carrión's experience in Puerto Rico has been somewhat similar. I recall that he mentioned lupus erythematosus as another disease to be considered in the differential diagnosis.

It is rather singular that in the reports which have come from the locality in which the condition was originally observed, namely, Brazil, there has been such a paucity of references to other than the typical verrucous form. I doubt that there is truly a paucity of cases of other types of the condition. I have a feeling that if fellow Americans in Brazil were to go into the subject as exhaustively as Dr. Pardo-Castello has, these other clinical forms of chromoblastomycosis would be uncovered.

Excepting only Lane's case, all of the 7 cases in the United States have been encountered within the last ten years, and it is rather curious that in this audience today there are several members who have had more or less intimate experience with chromoblastomycosis. Lane reported the first case in the United States, from Boston; Martin Engman Jr. was closely associated with the case reported from St. Louis; the Haileys reported a case from Atlanta, Ga.; Sams, from Miami, Fla., and Weidman and Rosenthal, from Philadelphia.

In respect to therapy, there is much difference of opinion. By and large, pessimism dominates, but I do not think that the door is altogether closed to possibilities for successfully combating this condition. Perhaps most of the unfavorable ideas about treatment have been predicated on results in cases of extreme, advanced condition. In the case from Philadelphia the condition cleared up materially with iodide therapy and small, insufficient doses of roentgen rays. As I recall, the condition in the case from St. Louis was cured. In both of these cases the condition was in extremely early stages; so it may be that provided the condition is diagnosed early and properly treated there may be some hope. Incidentally, it cannot be expected to be detected in the early stages unless physicians are on the alert to recognize conditions that for the moment may pass as some form of tuberculosis or syphilis.

Dr. Braulio Sáenz, Habana, Cuba: I wish to speak in regard to the high incidence of chromoblastomycosis in my country. In the last year about 6 cases of this condition have been observed in my department at the Mercedes Hospital. Dr. J. Castro-Palomino and Dr. J. Alfonso Armenteros, in charge of the mycologic study of these cases, stated that Phialophora verrucosa was the responsible organism. The recognition of chromoblastomycosis in Cuba is of relatively recent date, about five years ago. Prior to that time in most of the cases the condition had been interpreted as Gilchrist's dermatitis.

In 2 of our cases there were periosteal alterations of the lower extremities, where the lesions were located. Hypochromic anemia was also a common feature.

After the administration of iodide potassium, suppression of sodium chloride in the diet and administration of epinephrine increase the good results and also the tolerance of the drug. When these drugs fail, electrocoagulation and roentgen therapy prove helpful.

LUPUS ERYTHEMATOSUS HYPERTROPHICUS ET PROFUNDUS

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NEW YORK

The object of this paper is to discuss a variant of lupus erythematosus that has not been described. In fact, it is apparently so rare that no reference to it occurs in either the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY from 1911 to date or the Year Book of Dermatology and Syphilology from 1916 to date. It is not mentioned in the latest editions of American textbooks on dermatology. However, I did find a definite reference to it in the book on dermatotherapy by Sulzberger and Wolf.[1]

Until a better designation is found, I believe that the name already given it is fairly descriptive, namely, lupus erythematosus hypertrophicus. As, besides the characteristic hypertrophy, there is also a deep infiltration, "et profundus" should be added to the name. Despite the almost complete absence of reports of it in the literature, this variant of lupus erythematosus is known to many dermatologists, and the only claim I make for originality in presenting it is that I believe this is the first time an attempt has been made to define it clearly and to differentiate it from other variants with almost similar names.

The symptoms of lupus erythematosus hypertrophicus et profundus are definite. The only variation in the clinical picture is the degree of severity of the lesions. It belongs to the fixed discoid variety. A typical example is characterized by more or less oval, rather sharply outlined, greatly elevated, plateau-like plaques with indurated rolled borders and varying from violaceous to dull red. The surface of the plaque is at times covered with thick adherent scales. The center of the plaque is depressed, and extensive atrophy, occasionally cribriform, is present. At other times the plaque is covered with a thick, dry, digitate, verrucous-like, hyperkeratotic layer. These oval plaques at times coalesce to form larger areas. On palpation they have a cartilaginous feel, and when single a plaque bears a rough resemblance to a large slowly growing basal cell epithelioma of the elevated variety. The plaques have a tendency to heal centrally, and while they have been

Read at the Sixty-Fourth Annual Meeting of the American Dermatological Association, Inc., New Orleans, April 9, 1941.

1. Sulzberger, M. B., and Wolf, J.: Dermatologic Therapy in General Practice, Chicago, The Year Book Publishers, Inc., 1940, p. 494.

observed on the upper part of the face, their sites of predilection are the lower lip, the sides of the mouth and the chin. When the lip is involved, it is usually the entire lower lip, thereby greatly disfiguring the patient. Again the diseased area may not be confined to the lip alone but may spread well beyond the vermilion border. As the lesions undergo involution, they at times leave mutilating, unsightly areas of atrophy. In a case which came under my observation, the mutilation

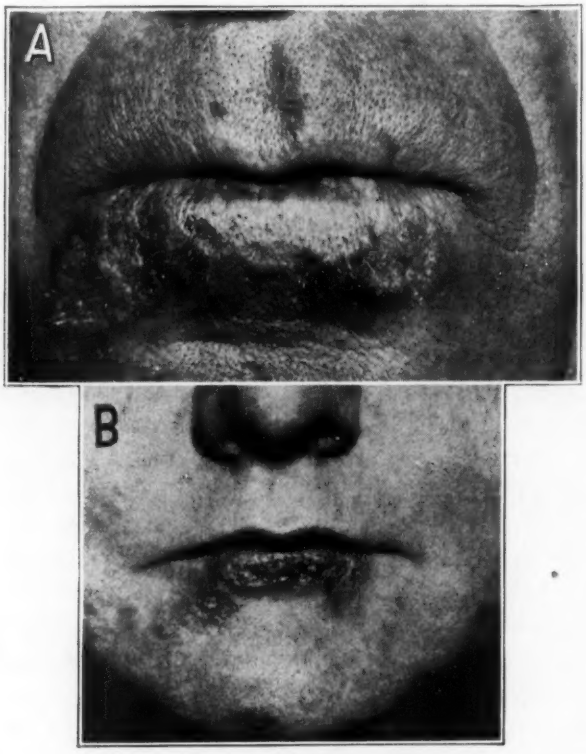

Fig. 1.—*A*, lupus erythematosus hypertrophicus et profundus showing indurated rolled borders. *B* shows the favorite site of such lesions and typical cribriform atrophy.

of the nose was so great that it left a deep punched-out scar, just as though the nose had been bitten by a sharp-toothed animal.

The disease in question must be differentiated from other variations of lupus erythematosus which bear a rough resemblance to it. Lupus erythematosus profundus of Irgang,[2] for example, must be considered. His patient had four pinhead-sized to split pea–sized red superficial

2. Irgang, S.: Lupus Erythematosus Profundus, Arch. Dermat. & Syph. **42**:97 (July) 1940.

lesions on the right cheek, a similar lesion on the left cheek and a flat, smooth, subcutaneous, flesh-colored plaque about the size of a 50 cent piece on the left shoulder, a totally different clinical picture from that of lupus erythematosus hypertrophicus. Jamieson [3] presented before the Detroit Dermatological Society a patient with large erythematosquamous plaques of lupus erythematosus with a distinctly verrucous appearance on the nose, cheeks, ears and backs of the hands. The short clinical description does not coincide with that of lupus erythematosus hypertrophicus. Pautrier [4] expressed the opinion that Brocq's *lupus erythémateux profound* was lupus vulgaris, an opinion later shared by Brocq, as the latter omitted a description of this condition in his chapters on lupus erythematosus in his "Traité élémentaire de dermatologie practique." Under the name of lupus erythematodes tumidus, Gougerot and Burnier [5] described red patches of a soft consistency with a smooth red surface. These patches were circinated or oval, sharply outlined and most frequently observed on the neck. Follicular hyperkeratosis was absent. This is a clinical description which does not at all tally with lupus erythematosus hypertrophicus. While there is much confusion in the differential diagnosis between the early stages of Boeck's sarcoid and lupus erythematosus, this does not hold true of the hypertrophic type. The yellowish red to brownish red cutaneous and subcutaneous plaques of multiple benign sarcoid with their smooth surfaces and soft infiltration do not at all resemble lupus erythematosus hypertrophicus. The same holds true of the Darier-Roussy, the Spiegler-Fendt and the generalized type of sarcoidosis. Angiolupoid of Brocq and Pautrier was described by Pautrier as a roundish or oval plaque, almost flush with the skin, of violaceous red with yellow marbling. On diascopic pressure the redness disappears and the yellow remains. The surface of the plaque is shiny and smooth, without a trace of scaling. It is thinned but not atrophic. Telangiectasia is present. On palpation there is a sensation of extremely soft infiltration. This classic description by Pautrier, as will readily be noted, does not at all resemble lupus erythematosus hypertrophicus.

I have observed a number of instances of the hypertrophic type of lupus erythematosus, the symptoms being exactly the same in all cases except for the degree of severity. A report of my 2 most recent cases follows:

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3. Jamieson, R. C.: Verrucous Lupus Erythematosus, Arch. Dermat. & Syph. **13**:293 (Feb.) 1926.

4. Pautrier, L. M., in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 3, p. 747.

5. Gougerot, H., and Burnier: Lupus erythematodes tumidus, Arch. dermatosyph. Clin. Hôp. Saint-Louis **3**:273, 1931.

REPORT OF CASES

CASE 1.—F. S., a man aged 49, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, was presented by me at a meeting of the New York Dermatological Society on Jan. 23, 1940.[6] He stated that his eruption had been present for two and one-half years. The lesions consisted of three oval areas, more or less confluent, situated on or about the lower lip and involving most of that area. They were dull red, raised and greatly indurated, with rolled borders. The central portions were atrophic, scaly and hyperkeratotic. The Wassermann and Kahn reactions were negative. The

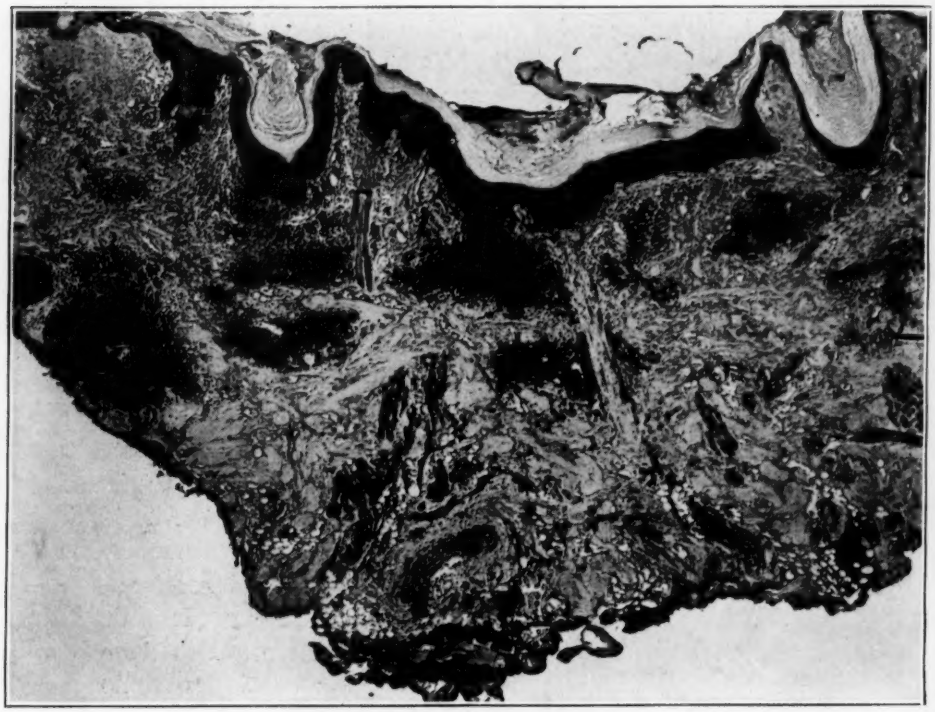

Fig. 2 (case 1).—Photomicrograph showing infiltration of lymphocytes in the corium and dilatation of the follicular orifices (× 75).

differential blood count was normal. A urinalysis showed no abnormalities. The patient did not return to the clinic for treatment.

Histologic examination was made by Drs. Satenstein and Sachs, who reported as follows: "Throughout the upper part of cutis and about the adnexa there is a tremendous cellular infiltration. The vessels in the papillary bodies and in the upper and middle parts of the cutis are dilated, and some are filled with blood elements. In the subepidermic region there is a pronounced basophilic degeneration. In the deep part of the cutis and extending almost up to, and

6. Bechet, P. E.: Hypertrophic Lupus Erythematosus, Arch. Dermat. & Syph. **42**:211 (July) 1940.

in places actually up to, the epidermis, there is striped muscle tissue. In the center of the section is a greatly dilated sweat duct and sweat gland. There is some interstitial edema throughout the cutis. The cellular infiltrate is composed of small round cells and wandering connective tissue cells. Throughout the upper part of the cutis the elastic tissue is missing, and there are large clumps of connective tissue directly beneath the epidermis. The epidermis for the most part

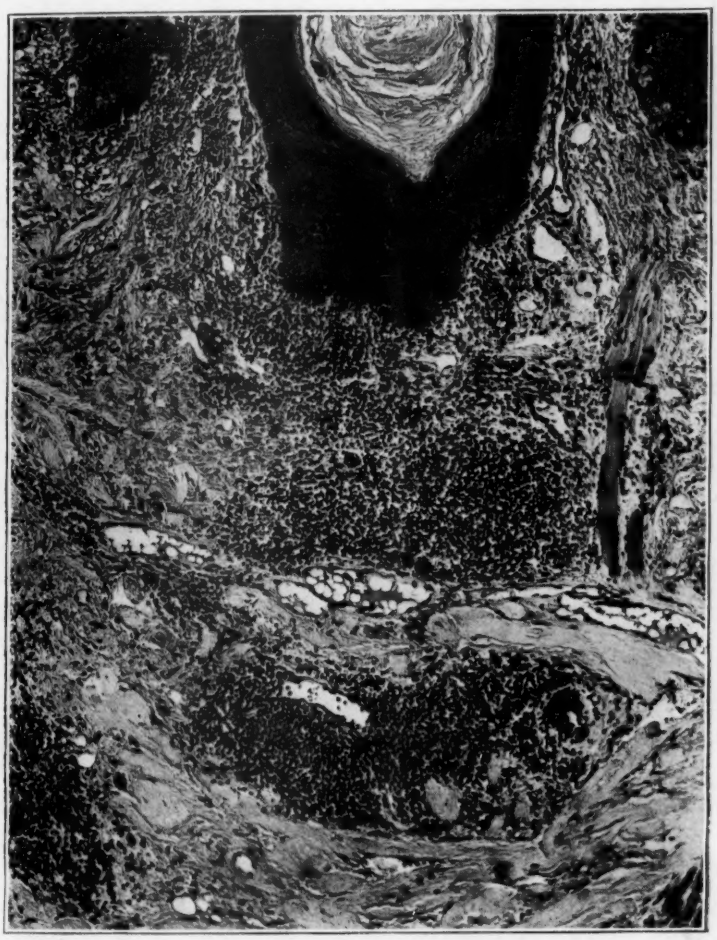

Fig. 3 (case 2).—Photomicrograph showing infiltration below the base of a dilated follicle. To the right is a bundle of skeletal muscle fibers (× 350).

is moderately acanthotic. The follicles are dilated and filled with densely laminated horny material. There are no other important changes within the epidermis."

Case 2.—M. P., a woman aged 29, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in January 1939 for the relief of a patch just below the vermilion border of her lower lip which had

been present for two years. It measured about 2 by 4 cm. On the right side of this patch and just below it was a much smaller one, about the size of a large lima bean. The large patch was raised, greatly infiltrated and violaceous red, with a depressed cribriform atrophic center. The smaller spot, apparently a more recent one, was also raised, infiltrated and violaceous. Central atrophy could be observed. The Wassermann and Kahn reactions were negative. The patient had received an undetermined dose of a bismuth compound intravenously at weekly intervals, approximately seventeen injections, prior to her visit to the clinic. She stated that she had noticed some improvement. After only six weekly intravenous injections of gold sodium thiosulfate, in doses beginning with 5 mg. and with a maximum of 30 mg., she disappeared from observation.

Histologic examination was made by Drs. Satenstein and Sachs, who reported as follows: "The vessels of the upper and middle parts of the cutis are dilated. In the upper part of the cutis there are several dilated lymphatics. There is considerable striped muscle in the deep portion of the cutis as well as in the midcutis and in places in the upper portion. There is a pronounced cellular infiltration about the vessels and also about the muscle tissue in the deep part of the cutis. The cellular infiltration is composed of small round cells, wandering connective tissue cells and a few plasma cells. There is some basophilic degeneration in the subepidermic zone. Elastic tissue is arranged in masses in the subepidermic region. In the midcutis the elastic tissue is fragmented. The epidermis shows no important change except dilatation of the follicle, within which is a densely laminated horny plug. At one point there is a suggestion of pearl formation, but this is probably a cross section of a hair follicle."

TREATMENT

Lupus erythematosus hypertrophicus et profundus is notoriously recalcitrant to treatment, even more so than lupus erythematosus of the lower lids. Yet, in my experience persistent treatment eventually brings about satisfactory results, particularly if the doses of either gold or bismuth are kept as high as possible with safety. In other words, success depends on maximum doses and lengthy treatment. I shall not enter into a discussion of the relative merits of gold or bismuth in lupus erythematosus, as it is not pertinent to this paper, but in this particular type of lupus erythematosus I have observed more frequent improvement when a gold preparation has been used.

I always use gold and sodium thiosulfate. The first dose is 5 mg., and in the absence of reactions, leukopenia, pruritus or dermatitis the dose is raised weekly to 10, 25, 50 or a maximum of 100 mg. Leukocytic counts are made at frequent intervals. In this way I have given sometimes as many as thirty to sixty or more injections of 100 mg., without accident. I have found that at times extensive improvement does not begin until many injections have been given; so I do not discontinue aurotherapy because of nonimprovement until at least twenty-five injections have been given.

SUMMARY

The clinical picture of lupus erythematosus hypertrophicus et profundus is uniform, definite and distinctive, sufficiently so in my opinion to establish it as a recognizable variant of lupus erythematosus. Its differential diagnosis from Boeck's sarcoid, lupus erythematosus profundus, angiolupoid and other variants is clinically possible.

ABSTRACT OF DISCUSSION

DR. EDWARD F. CORSON, Philadelphia: May I offer a brief exposition of the therapy in such a case, possibly the same one that Dr. Bechet mentioned as having been observed at the Philadelphia meeting (Jones, H. W.; Tocantins, L. M., and Corson, E. F.: Purpura Hemorrhagica Produced by Gold Salts, *Pennsylvania M. J.* **37**:809 [July] 1934)? This patient at the beginning of her second series of injections of a gold compound had hemorrhagic purpura. She was fearfully ill, but in a few weeks, thanks to the intervention of my hematologic confrères, she recovered, and the lupus erythematosus was found to have entirely disappeared. In the course of three years she suffered a relapse, with changes such as those seen in the slides and mentioned by Dr. Bechet. She presented an exaggerated example of such a condition. She was treated no longer by internal medication, for I feared any metallic treatment, even a bismuth compound. Application of solid carbon dioxide and of trichloroacetic acid had no effect. She was treated successively by several Philadelphia dermatologists, and eventually electrocoagulation gave good results. There was considerable scarring, but on the whole the end result was good. After hearing Dr. Bechet's remarks, however, and assuming that the lesions may clear up spontaneously, I wonder how much nature had to do with the result.

DR. PAUL E. BECHET, New York: In answer to Dr. Corson, I am sorry that he was under the impression that I said that involution was spontaneous. On the contrary, I specifically stated that this type of lupus erythematosus was most recalcitrant to treatment and required prolonged aurotherapy for several months in order to attain a good result and that even after healing a disfiguring atrophy was always present.

NECROBIOSIS LIPOIDICA AND GRANULOMA ANNULARE

A COMPARATIVE STUDY

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AND
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A review of the literature on necrobiosis lipoidica disclosed that a few investigators [1] have expressed the opinion that granuloma annulare and necrobiosis lipoidica may be closely related diseases. One of us (F. A. E.) presented evidence suggesting that many cases presented under titles such as "sarcoid" or "tuberculosis with sclerodermatous changes" should have been classified as instances of necrobiosis lipoidica or granuloma annulare. The present study consists of: (*a*) a consideration of the hitherto generally or commonly accepted concepts of the two diseases; (*b*) a review of the literature and critical analysis of the cases presented as instances of necrobiosis lipoidica and an analysis of the cases of granuloma annulare in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY from 1930 to 1940; (*c*) an analysis of clinical features of a group of 43 patients observed by us at the Johns Hopkins Hospital, the University of Maryland Hospital and in our private practices, and (*d*) a critical appraisal of the histologic material which has been gathered during the past fourteen years by the dermatologic department of the Johns Hopkins Hospital from patients with a diagnosis of necrobiosis lipoidica or granuloma annulare. When the data from the literature were correlated with our own data the similarity of many features of the two entities was striking.

Granuloma annulare has been described as a chronic inflammatory dermatosis characterized by deep-seated, white, pink or rarely purple, flat-topped, raised nodules of a firm or doughy consistency, which spread peripherally to form annular lesions. They vary in size from 1 to 8 cm., but occasionally larger plaques may be formed by the confluence of several smaller plaques. The lesion usually occurs on the upper extrem-

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From the Department of Dermatology, Johns Hopkins University School of Medicine.

Read before the Section of Dermatology and Syphilology at the Ninety-Second Annual Meeting of the American Medical Association, Cleveland, June 4, 1941.

1. Bernstein, Boldt and Traub (references *c* and *f*).

ities. Dermatologists generally recognize the classic textbook description of granuloma annulare and consider that its gross morphologic features are easily differentiated from those of necrobiosis lipoidica. However, Hyde described the lesion of granuloma annulare as a plaque with a lucent sclerotic surface and in some instances a dark or violaceous outer zone.

Necrobiosis lipoidica has been described as a chronic disease of the skin which occurs usually on the lower extremities and is characterized by flat or slightly raised violet plaques, with dull red or bluish red borders and yellow centers. The early lesion is a sharply demarcated, distinctly elevated red papule, whereas the well developed lesion is a round, oval or irregularly shaped plaque with a smooth glistening or waxy surface and a central portion that may be slightly raised or atrophic and of a cartilaginous texture or that may be coppery or xanthochromic and traversed by telangiectases. Lesions vary in size from 0.5 to 8 to 10 cm. in diameter. Single plaques may fuse to form larger plaques. Oppenheim (reference *c*) described several stages: First there is a firm, small, flat, red papule; as it enlarges a yellow center develops, which later becomes atrophic or necrotic, and this results in the formation of concentric or target-like figures. Hitch's concept was similar, but he differentiated four stages. Riehl stressed the polycylic configuration and described a brown to livid red border 3 to 5 mm. wide and a well defined yellow center with telangiectasia covered by a slight scale. Madden stated that there may be a raised border like that seen in granuloma annulare.

SEX

In the literature 90 per cent of the 89 patients with a diagnosis of necrobiosis lipoidica were females, and in Joslin's unpublished series of 23 patients with necrobiosis lipoidica, 65 per cent were females. In the review of the cases of granuloma annulare from the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, 76 per cent were in females. In Jacobi's series of 24 cases of granuloma annulare only 57 per cent were in females. In our series of cases with a diagnosis of granuloma annulare by previous standards 83 per cent were in females.

AGE

The average age of the patients with necrobiosis lipoidica cited in the literature was 43 years. In 1937 Marble reported on 9 patients from Joslin's clinic with necrobiosis lipoidica. All except 2 were less than 25 years old. In Joslin's group of 23 cases the average age was 24.5 years. For granuloma annulare the average age of the patients cited in the ARCHIVES from 1930 to 1940 was 23 years. In our group the average age was 24, and 77 per cent of Jacobi's patients were less than

30 years old. Thus far the youngest patient with necrobiosis lipoidica reported on was 10 years old. Joslin's youngest patient was 9 years old. By contrast, 8 of the patients of our group with a diagnosis of granuloma annulare were less than 10 years of age and the youngest was 4 years old. The youngest patient with a diagnosis of granuloma annulare in the literature was 2 years old. In 20 per cent of the case reports reviewed in the ARCHIVES the patients were less than 10 years of age.

LOCATION OF THE LESIONS

In 80 per cent of the patients with a diagnosis of necrobiosis lipoidica described in the literature the lesions occurred on the lower extremity. In our group of patients with granuloma annulare 28 per cent had lesions on the lower extremity and 70 per cent on the upper extremity. Jacobi stated that usually the lesions of granuloma annulare occur on the dorsa of the hands. In the cases reported in the ARCHIVES from 1930 to 1940 60 per cent of the lesions were on the upper extremities. Nine per cent of the patients had lesions about the head and neck, 20 per cent had generalized lesions and 40 per cent had lesions on the lower extremities. It was noteworthy that when granuloma annulare occurred on the lower extremity the patient was frequently less than 10 years of age. Necrobiosis lipoidica has been reported on the ear, face, back, chest, axillas and abdomen, while granuloma annulare has occurred in similar areas in our group of cases. In the cases reported in the literature practically every part of the cutaneous surface has been involved.

COURSE

In 9 patients with necrobiosis lipoidica the lesions were said to have undergone involution; 6 of these were considered to have responded to dietary control of the concomitant diabetes. Traub and Vero mentioned 2 cases in which the lesions underwent involution following biopsy. Complete healing occurred in six months under dietary control in the case with features common to both diseases reported by Ellis. In Boldt's fourteenth case (reference *a*) the lesion underwent complete healing in one year. In case 3 of our report the lesions underwent involution after treatment with divided doses of lightly filtered roentgen rays; there has been no recurrence, and the patient has not shown any evidence of diabetes after seven years. Jacobi stated that the lesions in 1 of his patients with granuloma annulare persisted for twenty-seven years. Ulceration was observed in 17 cases of necrobiosis lipoidica. The ulcerations may be fortuitous due to the lowered resistance of the patient, trauma and location of the involved areas. In Balbi's patient the ulcerations were extensive, suggesting the possibility that a secondary infection might have been superimposed on the original condition. In

only 1 of our group of patients with a diagnosis of granuloma annulare was an ulcer seen. Atrophy was noted in lesions of 4 patients.

NUMBER OF LESIONS

Granuloma annulare may occur as single or multiple lesions, and occasionally they are numerous; likewise, necrobiosis lipoidica may be characterized by single or multiple lesions. Boldt (reference *a*) stated that as many as fifty lesions have been present in 1 patient.

FREQUENCY OF ASSOCIATED DIABETES

Oppenheim (reference *a*) and Urbach (reference *a*) originally reported cases of necrobiosis lipoidica in patients with diabetes. As more examples of the disease were observed, diabetes was found to be present less often, and therefore the term necrobiosis lipoidica diabeticorum may be considered incorrect. Twenty-nine cases (30 per cent) have been reported in which the patients were nondiabetic. Forty-three per cent of Boldt's patients did not have diabetes, and 40 per cent of our patients with necrobiosis lipoidica were nondiabetic. Boldt stated that the complication of diabetes seemed to aggravate the lesions. Other investigators have maintained that when diabetes mellitus was not demonstrable it was latent and would become apparent later in life. Trauma has been considered by many investigators to be an etiologic factor in necrobiosis lipoidica, but it has not been suggested as a causative factor in granuloma annulare.

CHEMICAL EXAMINATION OF THE BLOOD

Urbach found that the blood lipoid values were increased in patients with necrobiosis lipoidica. Gottron (reference *a*) considered necrobiosis lipoidica to be due to a local fat disturbance following a general fat dysfunction; however, he observed that hypercholesteremia or hyperlipemia was not necessarily always present. Hildebrand's studies of blood lipoids showed no essential abnormalities. Joslin stated that less than 5 per cent of his diabetic patients in whom blood lipoids were studied had a hypercholesteremia and that the lipoids were usually increased only in the patients with uncontrolled diabetes. No studies of the blood lipoids in patients with a diagnosis of granuloma annulare have been found in the literature, but in the few studies made by us there were normal values.

COMPARISON OF THE HISTOLOGIC PICTURE OF THE TWO DISEASES

The epidermis in both dermatoses is usually normal or shows evidence of slight atrophy, which is apt to be more evident in necrobiosis lipoidica. In both diseases, in the subepidermal or the superficial layer

of the cutis, the capillaries are dilated and surrounded by a light mantle of lymphocytes.

Changes in the Connective Tissue.—In necrobiosis lipoidica the most characteristic change is the degenerative or altered appearance of the connective tissue in the cutis. The changed collagen bundles have been described as necrotic, sclerotic, necrobiotic, acellular and homogeneous. Oppenheim stated that in necrobiosis lipoidica the connective tissue formed anuclear flakes and "chunks" which were more or less eosinophilic rather than normal connective tissue. In sections stained by the Van Gieson method he found the altered collagen yellowish brown and the elastic tissue destroyed. Sections from an early lesion of necrobiosis lipoidica in our series revealed acellular collagen which retained its normal staining property and shape. Fairly well preserved infiltrative cells were observed frequently in the necrobiotic areas, and in some cases many basophilic nuclear fragments. In the late or final stage there were large well defined areas of moderately homogenous acellular collagen. However, in the areas with the most advanced alteration, the collagen fibers were usually present in their normal forms or with only slight alteration of their architecture. In a few cases the fibers were narrowed and stained poorly or had a glassy appearance. In small areas parts of the collagen fibers were fragmented, granular or relatively homogeneous. These changes are associated with necrosis, but the areas so altered were always relatively small regardless of the duration or extent of the lesion. Many variations from this picture were noted, such as basophilic strands of collagen interspersed between the eosinophilic or poorly stained and greatly altered fibers.

In sections from patients with a diagnosis of granuloma annulare the collagen changes were similar and varied only in degree. If large areas of necrobiosis were present the collagen was acellular, "glassy" and fragmented and resembled that observed in necrobiosis lipoidica. There were usually numerous smaller areas of altered collagen in which these changes were not so extensive or so far advanced. In a single high power field granular collagen was interspersed among structurally fairly well preserved basophilic collagen and short strands of normally staining eosinophilic bundles. In these areas infiltrative cells were observed and/or varying amounts of nuclear debris. At the border of the infiltrate and extending into the zone of altered collagen there were frequently noted areas of slightly basophilic collagen surrounding the epithelioid cells. Similar changes were usually present in sections of necrobiosis lipoidica at the zone of infiltrate in juxtaposition to the zone of sclerotic connective tissue. The finer details of the aforementioned changes may be distorted or lost if the tissue has been subjected to harsh fixatives or if a good technic has not been followed in preparing the sections.

Goodman and Ketron stated that as the degeneration process advanced in granuloma annulare the infiltrative cells died, leaving areas containing a variable amount of pyknotic nuclei and chromatin dust. They further stated that the changes in the connective tissue may proceed to complete degeneration of all the fibrils, leaving only a granular substance with or without nuclear remains, but in most of their material partially preserved bundles of connective tissue were present and the elastic tissue was not electively affected. In both diseases the degenerative changes in the elastic tissue preceded that of the collagen; it was more extensively altered than the collagen fibers.

Palisading.—In granuloma annulare the arrangement of the infiltrating cells at the border of the collagen has been the subject of much comment. In this disease the palisading of the epithelioid cells is usually considered a pathognomonic histologic change. Goodman and Ketron cited Hopkins' case of a juxta-articular nodule in which palisading of the infiltrate around a necrotic area was as striking as that seen in granuloma annulare. Boldt reported palisading of the infiltrating cells in necrobiosis lipoidica. Figure 4 in the article by Hitch and figure 2 of the report by Ellis portrayed palisading (?) of the lipoids. In 70 per cent of our group of patients with necrobiosis lipoidica there was moderate palisading; it was less characteristic than that observed in patients with a diagnosis of granuloma annulare. In granuloma annulare palisading was observed in some areas in practically all of the sections. It is our impression from a study of the available sections that palisading was not as well developed in necrobiosis lipoidica as in granuloma annulare. Nevertheless, sections from patients with necrobiosis lipoidica may show in some areas evidence of this arrangement. The infiltrating fibroblasts or epithelioid cells frequently were arranged with their long axes lying in parallel strands or columns.

Infiltrate.—In thirty-seven articles on necrobiosis lipoidica the different types of infiltrating cells were mentioned as follows: lymphocytes, in twenty-six (70 per cent); the foreign body type of giant cell, seventeen (46 per cent); fibroblasts, sixteen (43 per cent); plasma cells, eight (21 per cent); histiocytes, six (16 per cent); endothelioid or epithelioid cells, five (12 per cent), and the tuberculous giant cells, four (10 per cent). Macrophages, polymorphonuclear eosinophilic leukocytes and reticuloendothelial cells were mentioned once or twice. Two investigators found calcium in the altered collagen.

All of the sections from patients with lesions of necrobiosis lipoidica examined by us contained epithelioid cells and lymphocytes. Nuclear debris was observed in 45 per cent, and there were many fibroblasts in 30 per cent of the sections. In more than half the cases there were giant cells of the foreign body or Langhans type; neither type predomi-

nated. Two sections showed plasma cells and two polymorphonuclear neutrophilic and eosinophilic leukocytes. The infiltrate surrounded the areas of degenerated collagen in a poorly defined band. There were two types of well defined infiltrate not adjacent to the zones of necrobiosis. One consisted principally of a well defined collection of closely packed small mononuclear round cells (lymphocytes) which surrounded many small blood vessels and the capillaries. The other type was made up of epithelioid cells, lymphocytes, fibroblasts and other less frequently seen infiltrative cells, such as the plasma cells and polymorphonuclear leukocytes. Giant cells were often found in the latter type of infiltrate. At times a sarcoid-like architecture occurred in these areas.

In all of the sections from patients with granuloma annulare small lymphocytes and epithelioid cells were present in varying degrees. There were some fibroblasts in the majority of the sections; in a few the fibroblasts were more numerous than the epithelioid cells. In granuloma annulare nuclear debris was less abudant than in necrobiosis lipoidica. The cells less frequently present, such as plasma cells, polymorphonuclear neutrophilic and eosinophilic leukocytes, were seen in about the same proportion in granuloma annulare as in necrobiosis lipoidica. The surprising observation was the infrequent presence of giant cells in granuloma annulare; they were found only twice (7 per cent). By contrast, in necrobiosis lipoidica giant cells of various types were found in 56 per cent of the cases in the literature and in 50 to 60 per cent of the sections in our cases.

Vascular Changes.—Boldt (reference *c*), Michelson and Laymon, Zeisler and Caro and others have stressed the etiologic significance of the vascular alterations in necrobiosis lipoidica. The vascular changes have been compared with those associated with arteriosclerosis and diabetes. On the other hand, Jacobi stated that in granuloma annulare there was a new capillary growth and proliferation of the endothelium of the veins which sometimes resulted in occlusion of their lumens but caused no alteration in the arteries. However, he described a deep type with arterial vascular changes and occlusion of the vessels. He concluded that the primary pathologic process was apparently endovascular and perivascular, resulting in complete obliteration of the vessels with necrosis (?). Goodman and Ketron found a more or less pronounced inflammatory reaction surrounding the blood vessels in cases of granuloma annulare. In few of the circumscribed areas of degeneration were they able to find either normal or degenerated vessels; in only 1 case were important changes seen in the vascular branches. The walls of the blood vessels were thickened as a result of endothelial proliferation and a varying amount of fibrosis. They stated that this resulted secondarily in atresia or occlusion of the lumens.

Because of the variations, it was difficult to appraise and summarize the vascular changes in our series of cases. The vessels in the cutis were relatively small and usually showed only slight perivascular and mural fibrosis or endothelial proliferation. In most of the biopsy specimens the subcutaneous tissue which contained the larger vessels was not included. The deeper vessels had thickened walls which usually showed some fibrosis and distortion of the vascular coats. Endothelial proliferation was not active except in some of the smaller vessels. The two types of perivascular infiltrates found in the cutis are discussed in detail under the infiltrative cells present in the case reports.

Biopsy specimens from 2 of our patients with a diagnosis of granuloma annulare included the panniculus, in which there was general and perivascular fibrosis in the upper layer of fat, and the adjacent lower part of the cutis. Several dermatohistologists who had examined the sections made a diagnosis of granuloma annulare in spite of the fact that there was more fibrosis than in any of the sections from our patients with necrobiosis lipoidica. One of the specimens was from the elbow of a 6 year old girl whose lesions disappeared soon after the biopsy was made.

It is our impression that the vascular changes and perivascular fibrosis at times may be as severe in sections from patients having granuloma annulare as in those with necrobiosis lipoidica.

REPORT OF CASES

CASE 1.—E. U. A., a white woman aged 35, was first seen on Jan. 20, 1940, complaining of a generalized eruption of two years' duration. The extensor surface of the forearms, the lower part of the back, the buttocks and the legs were involved by more than fifty lesions consisting of slightly raised moderately firm nodules or plaques of yellow to pale pink. There were many plaques on the elbows but only a few on the knees. On diascopic pressure a yellow to light brown color remained, but no apple jelly nodules were observed and many of the smaller nodules were obliterated completely. The largest plaque was about 2 cm. in diameter, but the majority of them were approximately 0.5 cm. in diameter. On the eyelids there were a few papules, several millimeters in diameter, which grossly resembled syringocystomas; there were no xanthelasmas.

The patient gave a past history of occasional attacks of "indigestion" and moderate drinking of alcohol for seven years. She had received roentgen ray treatments for maxillary sinusitis, and this resulted in some telangiectasia of the skin of the malar eminences.

The urine was essentially normal. Examination of the blood showed the following values: hemoglobin, 72 per cent (Dare); red cells, 3,720,000; white cells, 5,600; polymorphoneutrophilic leukocytes, 65 per cent; lymphocytes, 30 per cent, and monocytes, 5 per cent. The fasting blood sugar was 100 mg. per hundred cubic centimeters and the blood cholesterol was 252 mg.

A low fat diet was prescribed, and yellow and green foods were interdicted. The plaques were treated with 50 to 100 r of roentgen rays through 1 mm. of aluminum every five to ten days for a total dose of 580 r within six weeks. Involu-

tion rapidly followed. On March 15 it was noted that the plaques on the elbows were flat and that a slight residual brown had replaced the original yellow. At this time the lesions on the lower part of the back, the buttocks and the posterior and outer surfaces of the thighs were still slightly palpable.

Two biopsy specimens were obtained: the first was in January, before treatment, and the second was on March 30, after the majority of the plaques had undergone involution. The first specimen showed a normal epidermis and slight dilatation of the capillaries in the upper part of the cutis. In some very small areas the collagen was slightly granular and moderately basophilic. In other areas collagen fibers were thicker and more eosinophilic than those in the surrounding area. The infiltrate consisted principally of epithelioid cells which radiated from a center of altered collagen. Interspersed between the epithelioid cells there were many small lymphocytes and a few fibroblasts. The blood vessels

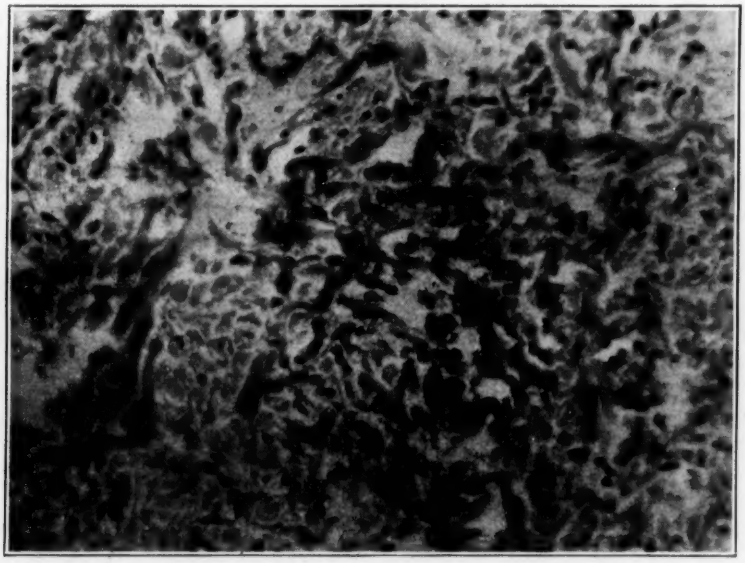

Fig. 1 (case 1).—Granuloma annulare, showing the type of infiltrate, consisting of lymphocytes, epithelioid cells and a few fibroblasts. Early collagen changes were present but are not demonstrable in the black and white photomicrograph.

near the area of infiltrate were dilated and surrounded by a light mantle of epithelioid cells, fibroblasts and lymphocytes. Approximately half of the largest area of infiltration was within a high power field. Staining with sudan III showed large moderately well defined areas containing rather closely packed sudanophilic globules varying in size up to about twice that of an epithelioid cell. It was not possible to determine whether the lipoid material was intracellular or extracellular, but it seemed to fill all the area except the open spaces which contained no cells or tissue. There were no xanthoma cells. The second specimen, taken ten weeks after the first, showed only a few fibroblasts in the upper layer of the cutis, and staining with sudan III showed no fat.

Our first impression was that the diagnosis was xanthoma; the histologic examination excluded this possibility. In retrospect, however, the yellow, firm,

waxy, slightly elevated papules or plaques were characteristic of granuloma annulare. The histologic appearance of the sections stained with hematoxylin and eosin was confirmatory, but we have never observed so much lipoid material in biopsy specimens from patients with this disease. The blood sugar and cholesterol values were within normal limits. The rapid response to roentgen ray therapy was compatible with the diagnosis of granuloma annulare.

CASE 2.—S. C., a white woman aged 48, was first seen on Jan. 30, 1940, because of a dermatitis venenata. Physical examination revealed a lesion on the anterior surface of the leg; according to the patient the eruption on the leg appeared in 1932, following an injury. Occasionally it was painful. There was no history of diabetes mellitus. The patient had had attacks of syncope, which were apparently relieved promptly by the ingestion of some form of carbohydrates. The lesion consisted of eight infiltrated plaques, which varied in size from 1 to 3 cm.

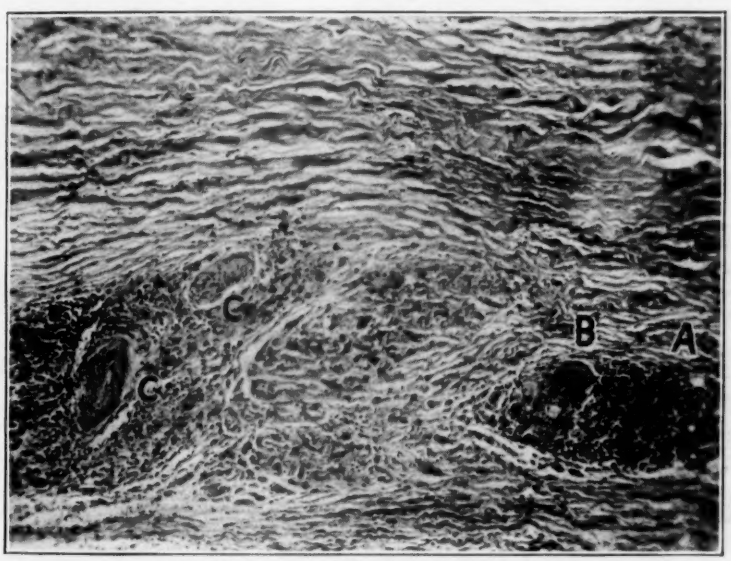

Fig. 2 (case 2).—Necrobiosis lipoidica, showing the loose, relatively acellular collagen split into fine ribbons. *A*, indicates a well defined collection of lymphocytes; *B*, tuberculoid architecture with giant cells; *C*, perivascular and intramural fibrosis of the walls of the blood vessels.

in diameter. They were irregularly oval, with well defined borders and a smooth glistening surface. From the periphery toward the center the color ranged from violaceous to yellow, and on diascopic examination the yellow was more prominent. The center of the larger plaques appeared slightly depressed and was traversed by numerous superficial telangiectatic vessels. There was no ulceration or scarring.

The urine was essentially normal. Chemical analysis of the blood after fasting gave the following values per hundred cubic centimeters: sugar 71 mg., cholesterol 174 mg., cholesterol esters 96 mg. and total fats (plasma) 680 mg.

A biopsy specimen was taken from the border of the larger lesion on the anterior surface of the left leg. Microscopic examination showed a normal

epidermis; in the subepidermal layer there were dilated capillaries with some perivascular infiltration. There were large areas of relatively acellular collagen. The fibers, on the whole, were only slightly paler than normal, but in many areas they seemed to be split into small fibrils, and in a few small areas there was granular degeneration. Slight nuclear debris was present in parts of the altered collagen. Surrounding the acellular collagen there was a moderately well defined infiltrate consisting principally of fibroblasts, lymphocytes and a few epithelioid cells. There was a suggestion of palisading in a few areas. In areas not adjacent to the altered collagen, especially deep in the cutis, there were well defined areas of perivascular infiltrate. The infiltrate consisted of poorly developed, foreign body and tuberculoid giant cells, epithelioid cells, plasma cells, fibroblasts and lymphocytes. Other areas of similar size contained numerous lymphocytes and plasma cells surrounding groups of small blood vessels or capillaries. The walls of the blood vessels, especially of the arteries, showed evidence of fibrosis and endothelial proliferation, so that atresia and occlusion of the lumens were seen.

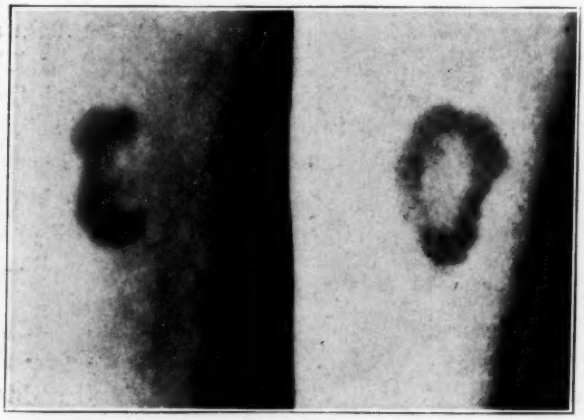

Fig. 3 (case 3).—Nondiabetic patient with necrobiosis lipoidica. Note the target-like figures forced by the slightly inflamed borders with telangiectasia and the yellow atrophic centers. Diascopic examination of the border disclosed a diffuse apple jelly color.

Staining with sudan III showed many small sudanophilic granules in the areas of acellular collagen. The sudanophilic globules were minute; the largest was the size of a nucleus of a lymphocyte. The globules were deposited in rows or strands following the pattern of the collagen fibers; they were denser in the central part of the necrobiotic tissue and absent in the areas of infiltration.

The diagnosis of necrobiosis lipoidica without diabetes was made.

The plaques on the legs were treated with roentgen rays filtered through 1 mm. of aluminum in small divided doses over a period of four months for a total of 1,200 r. This resulted in only slight, if any, involution of the plaques.

Case 3.—H. W., a white woman aged 35, was first seen at the University of Maryland Hospital in November 1933, complaining of a lesion (fig. 3) on the legs of twelve years' duration. A clinical diagnosis was made of sarcoid or tuberculosis with scleroderma-like changes. When a biopsy specimen from the

left leg was examined, the diagnosis of granuloma annulare was made. Microscopic examination of a specimen taken from the border of a lesion showed changes so similar to those seen in case 2 that a detailed description is deemed unnecessary. No stains for lipoids were applied. More recently the sections were observed by numerous dermatologists, and the consensus was that the diagnosis was necrobiosis lipoidica in a patient without diabetes.

From May to August 1934 the patient received ¼ skin unit of unfiltered roentgen rays (75 r) each week for sixteen weeks. At the end of the course of treatment there was only slight improvement, but two months later both lesions had undergone involution, leaving a slightly atrophic scar. When the patient was seen in July 1940 there were no signs of activity. In repeated urinalyses over a period of seven years there have been negative reactions to Benedict's test. The interpretation of the lesion illustrates the usual course of events that occurred before the syndrome of necrobiosis lipoidica was well recognized.

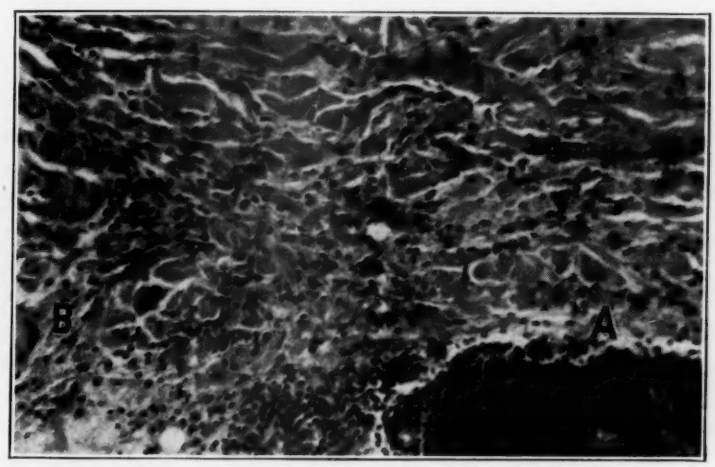

Fig. 4 (case 3).—An ill defined zone of infiltrate, consisting of lymphocytes, epithelioid cells and giant cells, surrounded the necrobiotic collagen. *A* indicates the dense well defined perivascular collection of lymphocytes as seen in both diseases; *B*, a giant cell.

SUMMARY

Granuloma annulare and necrobiosis lipoidica occur more frequently in females than in males. The early reports of cases of necrobiosis lipoidica suggested that the disease was one which occurred more often than granuloma annulare in older persons. As more case reports of the former syndrome have appeared, the age incidences of the "two diseases" have shown a tendency to approach one another. In both the lesions may be located on any part of the cutaneous surface. However, in patients with necrobiosis lipoidica the lower extremities were more often implicated, in contrast to the frequency of lesions on the upper extremities in patients with granuloma annulare. The number of lesions

in the two diseases are comparable; they may be single or multiple. Both diseases may be chronic. The duration of necrobiosis lipoidica is often longer than that of granuloma annulare. Approximately 10 per cent rapid cures have been observed in necrobiosis lipoidica. Atrophy or ulcers are occasional complications of necrobiosis lipoidica, but they are unusual in granuloma annulare. The presence of diabetes mellitus originally was considered a cardinal differential feature between these two diseases. Analysis of all cases thus far reported and of our cases of necrobiosis lipoidica and granuloma annulare showed that diabetes mellitus was associated with necrobiosis lipoidica in 73 per cent of the patients and that it occasionally complicated granuloma annulare. Histologically the two syndromes have many features in common. Slight or moderate epidermal atrophy has been reported more often in necrobiosis lipoidica than in granuloma annulare. Dilated capillaries and the other vascular alterations seen in both diseases may be indistinguishable. Fibrosis is often more advanced in sections from patients with necrobiosis lipoidica. The areas of necrobiosis are usually more extensive but less well defined in necrobiosis lipoidica. The types of infiltrative cells are similar in the two pathologic pictures. In necrobiosis lipoidica there are more fibroblasts and giant cells; i. e., there is a more chronic type of infiltrate. Small areas with a tuberculoid or sarcoid architecture usually are present. Pyknotic nuclei and cells and nuclear debris are observed in sections from patients reported to have either disease.

The presence of lipoid in the lesion has been considered a pathognomonic feature of necrobiosis lipoidica. Case 1 in this article was that of a patient with granuloma annulare. Large deposits of lipoids were demonstrated in the areas of infiltrate.

In summary the following differences seem to differentiate the two syndromes:

1. Necrobiosis lipoidica occurs in a possibly older age group.

2. There is a higher incidence of involvement of the lower extremities in necrobiosis lipoidica, in contrast to the higher incidence of involvement of the upper extremities in granuloma annulare.

3. There is a more chronic type of pathologic process in necrobiosis lipoidica, which results in more fibrosis and giant cells.

4. The areas of necrobiosis are less well defined in necrobiosis lipoidica.

5. Diabetes mellitus has been frequently associated with necrobiosis lipoidica and only occasionally with granuloma annulare.

6. The presence of lipoids in necrobiosis lipoidica was previously considered to be an absolute differential feature. The observations in case 1 in this report exclude this different point.

COMMENT

The study of the literature and of the data available to us suggest that the two syndromes may be variants of the same disease. The age of the patient, the location of the lesions, the circulatory changes, the presence of diabetes and the altered general and/or local lipoid metabolism may result in the different clinical and microscopic pictures. We are aware that two diseases may have many features in common and yet not be due to the same etiologic agent. For example, tuberculosis and syphilis are not considered to be closely related diseases, but at times they may be differentiated only with difficulty by the clinical and histologic pictures.

A trained observer can distinguish between the clinical and pathologic pictures of a classic case of necrobiosis lipoidica and one of granuloma

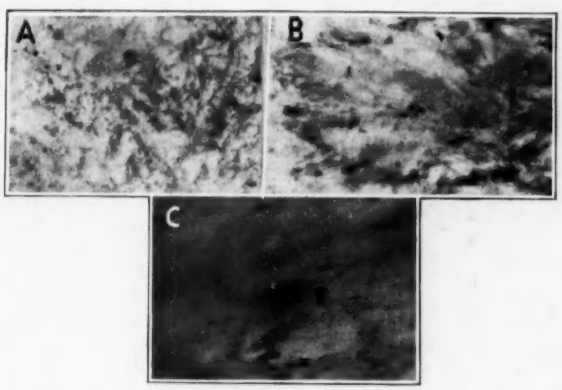

Fig. 5.—Sections stained with sudan III. *A* (case 1, low power), diffuse deposit of lipoids in the area of infiltrate. The large dark spots are artefacts (crystals). *B* (low power), from an early lesion of necrobiosis lipoidica, showing slight amount of lipoid in the area of advanced collagen changes and deposits at the zone of infiltrate, where early basophilic changes in the collagen have occurred. *C* (case 2), lipoid globules are relatively few and are present only in the altered collagen fibers (high power magnification).

annulare. A well defined zone of infiltrate with palisading surrounding a central area of fragmented, glassy, necrobiotic collagen is characteristic of the fully developed stage of granuloma annulare. By contrast, necrobiosis lipoidica, in the late stages, shows a less well defined zone of necrobiotic acellular collagen. The collagen fibers are usually less fragmented and not as glassy as those in granuloma annulare. The infiltrate does not surround the collagen in a well defined band but occurs mostly in moderately defined bands or zones. The infiltrative cells are of a more "chronic type" in necrobiosis lipoidica than in granuloma annulare. There was considerable disagreement when our sections from patients with the two diseases were submitted to several competent dermatohistopathologists.

CONCLUSIONS

1. Although the classic clinical and histologic features of granuloma annulare and necrobiosis lipoidica can be differentiated, there is some evidence that the two syndromes may be variants of the same disease.

2. Analysis of the case reports in the literature and a critical examination of the clinical and microscopic changes in patients observed by us demonstrated a striking similarity between necrobiosis lipoidica and granuloma annulare.

Fig. 6.—From a typical fully developed granuloma annulare lesion. The well defined zone of "glassy" necrobiotic collagen is surrounded by a zone of palisaded epithelioid cells and lymphocytes. *A* indicates a dense perivascular collection of lymphocytes in the subpapillary layer.

3. All of the clinical, histologic and histochemical features of necrobiosis lipoidica have at times been associated with granuloma annulare.

4. Clinical and microscopic variations may depend on the age of the patient, the location of the lesions and a general and/or local alteration of the lipoid metabolism. In the past such variations may have resulted in the conclusion that there were two distinct diseases, namely, necrobiosis lipoidica and granuloma annulare.

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ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: It is a radical departure to attempt to reconcile these two conditions which dermatologists have regarded for generations as separate clinical entities. That, however, cannot interfere with the work which Drs. Ellis and Kirby-Smith have done. Much depends on the sense with which the word disease is used in this presentation, that is, whether the word disease is predicated on a common etiologic factor or otherwise. In any event, in attempting to reconcile diseases, one cannot do so simply on the basis of histologic study; nor can one do so simply on the basis of the gross anatomy, the progress or any other single item except a common etiologic agent. It is necessary to consider all of the different phases of a given disease entity.

I agree entirely with the authors in respect to the histologic considerations, that is, as to the similarity of the histologic processes that are going on in the two conditions. Both of them are necrobiotic. There are reactions against that necrobiotic material in the form of so-called epithelioid cells. Palisading is common to them. There is, of course, a notable difference, namely, that fat is rather regularly developed as a consequence of degeneration and lipoidal changes in the case of necrobiosis, whereas in only 1 or 2 of Dr. Ellis' cases was fat present in granuloma annulare. But by and large, the order of histologic reaction is similar in these two conditions.

All dermatologists must agree that there are notable discrepancies as far as the gross morbid anatomy is concerned. As to the course—the progress of the disease—here also there are certain discrepancies. With all that in the picture, is it possible to reconcile these two conditions on the basis that the basic pathologic processes in the two conditions are the same but that in one there is a difference in the circumstance that the patient is diabetic? Can it be possible that in necrobiosis one is dealing with granuloma annulare in a diabetic subject? Unfortunately, that hope falls flat, because, as is well known, necrobiosis occurs in nondiabetic persons.

In short, it appears to me that it is not possible to reconcile these two conditions with the data at hand. There are serious hurdles which I personally cannot get over in respect to the anatomy in the case and in respect to the course of the disease processes. I do think, though, that a valuable message has come to us from this presentation, namely, as Dr. Ellis has shown, that the picture it not at all tuberculoid. I have felt for a long time, and I think the trend today is in that direction, that granuloma annulare is not tuberculous. At least, the histologic picture cannot influence one very far in that direction. My feeling has always been that the reaction in both granuloma annulare and necrobiosis lipoidica diabeticorum is only against the necrobiotic tissue, as in infarct of the spleen and of the kidney.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Dr. Prunty, under my supervision, has just completed a thesis, and he and I shall report 31 cases of granuloma annulare observed at the Mayo Clinic. Oppenheim has emphasized in discussions at meetings in the last few years that necrobiosis lipoidica is not a true necrosis of the connective tissue but a degenerative process. The same may be true of granuloma annulare, in which there is no true central caseation necrosis such as seen in certain types of tuberculosis. In several cases of necrobiosis staining

for mucin gave negative results. In all of our 13 cases of granuloma annulare in which histologic studies were made staining for mucin gave positive results. Staining for mucin, therefore, is probably of diagnostic value in distinguishing the two conditions. In a recent study of necrobiosis made with Drs. Hildebrand and Rynearson (Necrobiosis Lipoidica Diabeticorum, *Arch. Int. Med.* **66**:851-878 [Oct.] 1940), we found that in 80 per cent of the cases of necrobiosis the patients were women, in 90 per cent the patients were diabetic and in 18 per cent necrobiosis preceded evidence of diabetes by one to five years. It is my belief that in many of the 10 per cent in which there was no diabetes there may eventually prove to be diabetes. In regard to ganuloma annnulare, Dr. Prunty and I studied a total of 31 cases, in 11 of which the patients were under 9 years of age, the oldest being 57 and the youngest 1 year. Nineteen, or about 60 per cent, were females. Evidence of tuberculosis of the cervical glands was found in 1 of the cases of granuloma annulare. It is my belief that neither histologically nor clinically is granuloma annulare related to tuberculosis. In 1 case granuloma annulare was associated with diabetes mellitus. Staining for lipoids was not done in this case. In 1 case there was also associated lupus erythematosus. I am in agreement with the histologic changes of granuloma annulare, as shown in the authors' illustrations. I have not seen so many tuberculoid-like structures in the histologic changes in necrobiosis. I agree that the histologic picture of the two conditions may closely simulate one another, but clinically the two conditions are distinctive, and I believe granuloma annulare and necrobiosis are separate entities.

Dr. E. J. Eichenlaub, Washington, D. C.: Drs. Ellis and Kirby-Smith have done a careful and painstaking piece of histologic work and have made a careful search of the literature, but in spite of the fact that I have discussed the subject with Dr. Ellis personally and watched the work develop, I must say that I am not able to follow the argument. To my mind, these two diseases are so divergent clinically that the fact that there is some histologic similarity should not allow them to be classified as being in any way related. It is known—at least potentially definitely—what the basis for necrobiosis is; nothing at all is known about the cause of granuloma annulare, and the accidental occurrence of some fat in the two conditions seems to me to be not enough to associate the two diseases.

Dr. Francis A. Ellis, Baltimore: Dr. Oppenheim is correct in stating that in both diseases there is not a true necrosis but a necrobiosis.

As to the staining for mucin, I cannot answer; I have not tried it. Dr. Kirby-Smith and I think that the presence of diabetes does have something to do with the presence of fat in the tissue, but it is not a necessary factor.

We make a plea for the use of routine lipoid stains in all cases in which a diagnosis of granuloma annulare is considered. How many cases of granuloma annulare are encountered in a large diabetic clinic? It is odd that in Joslin's series there were 23 cases of necrobiosis lipoidica and apparently no cases of granuloma annulare. Would a study of the cases of granuloma annulare in diabetic subjects show the presence of lipoid material in the necrobiotic collagen and some of the other characteristics of necrobiosis lipoidica?

Dr. Weidman is correct; the tuberculoid architecture is a result of the altered collagen and the presence of lipoid material rather than an indication of a tuberculous causation. The clinical and microscopic variations may depend on the age of the patient, the location of the lesion and a general or local alteration of lipoid metabolism. Most lesions of necrobiosis lipoidica occur on the legs. One recognizes the variations in the clinical picture between papulonecrotic tuberculids and ecthyma on the legs in contrast to similar lesions seen on the upper extremities.

BACTERIAL FLORA OF THE NORMAL SKIN

REPORT ON THE EFFECT OF VARIOUS OINTMENTS AND SOLUTIONS, WITH COMMENTS ON THE CLINICAL SIGNIFICANCE OF THIS STUDY

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The relative effectiveness of various antiseptics commonly used in the treatment of superficial pyogenic infections of the skin is a subject of considerable conjecture and difference of opinion among clinicians. In another study we have attempted to determine whether or not there is any regular correlation between the bactericidal or bacteriostatic effects of various antiseptics in vitro and their clinical effects on the skin of the patient with impetigo, ecthyma, intertrigo, folliculitis and similar dermatoses in which pyococci play a role.[1] We were unable to demonstrate that in vitro studies are of great value in predicting the bactericidal action of an antiseptic on the skin.

The method devised by Price[2] offers a means of determining accurately the effect of various antiseptics in reducing the bacterial flora of the skin, and, to our knowledge, it has not previously been used in studying the antiseptic effects of ointments. Briefly, this method consists of a determination of the rate of removal of bacteria from the skin by a standard method of scrubbing with soap and water. With careful technic, a trained subject removes the bacteria from his skin at a regular

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From the Departments of Dermatology and Syphilology, John H. Stokes, M.D., Director, and the Pepper Laboratory, Herbert Fox, Director, of the Hospital of the University of Pennsylvania.

1. Livingood, C. S.; Pillsbury, D. M., and Nichols, A.: The Bactericidal Effects of Antiseptics Incorporated in Ointment Bases of Various Types: Comparison of Laboratory and Clinical Studies, to be published.

2. Price, P. B.: The Bacteriology of Normal Skin: A New Quantitative Test Applied to a Study of the Bacterial Flora and the Disinfectant Action of Mechanical Cleansing, J. Infect. Dis. **63**:301 (Nov.-Dec.) 1938.

rate, and the reduction in the bacteria produced by the application of an antiseptic is indicated by changes in the number of bacteria removed in successive scrubs. Certain minor modifications of Price's procedure were found necessary in adapting the method to a study of antiseptics incorporated in greasy bases.

METHOD OF STUDY

Principle.—Price [2] has shown that if a person scrubs his hands and forearms according to a standard technic for a given period, the number of bacteria removed may be determined with reasonable accuracy by plating a sample of the soapy solution of rinsing obtained, incubating for forty-eight hours and counting the number of colonies. When the subject scrubs for successive short periods, the number of bacteria removed is large in the initial basins but gradually falls. In a given experiment (chart 1) the number of bacteria removed in the initial basins may be of the order of 2,000,000, rapidly falling at first, until a relative plateau of the order of 240,000 bacteria per basin is reached. If an antiseptic is applied at some point during the series of scrubs the number of bacteria recovered in subsequent basins falls in relation to the effect of the antiseptic in reducing the residual bacterial flora of the skin; at least, such an interpretation seems possible providing the antiseptic does not simply form a relatively sterile thin coagulum on the cutaneous surface and providing the final concentration of the antiseptic in the basin is not sufficient to inhibit the growth of bacteria in vitro.

Material.—Basins: Enameled basins with a capacity of about 4 liters were used. They were sterilized by steam under pressure.

Water: Sterile distilled water was used. Sterility is not essential, but it was found that distilled water facilitated the removal of ointments, particularly wool fat or petrolatum, and that it offered a theoretic advantage in preventing the formation of insoluble calcium soaps, which Jones and Lorenz [3] have shown to afford a protective film on the skin under which bacteria grow readily. One liter was used for rinsing with each basin.

Soap: It was found that soap solution was more effective than bar or granulated soap in removing ointments from the skin. At first we thought that the use of a constant quantity of soap for each scrubbing, not possible when a soap bar was used, would be advantageous, but this did not prove to be the case. Nine cubic centimeters of soap solution, containing 3 Gm. of a commercial brand of soap flakes, was used for each scrub, half of this quantity being poured in each palm.

Brushes, Glassware and Culture Medium: We used the kind of brushes, glassware and culture medium specified by Price.[2]

Scrubbing.—Each hand and forearm was scrubbed for exactly thirty seconds, making a total of one minute for the two. Especial care was taken to scrub the

3. Jones, K. K., and Lorenz, M.: Relation of Calcium Soaps to Staphylococcal Infections of the Skin, J. Invest. Dermat. **4**:69 (Feb.) 1941.

palms and nails thoroughly. Rinsing of the hands and forearms required about thirty seconds, and, after practice, it was found that each scrubbing, including changing the basin and pouring the soap solution in the palm, could be completed in two minutes. About thirty minutes was required for the usual series of fifteen scrubbings. Prescrubbing for three minutes to remove a portion of the transient bacteria was ordinarily carried out.

Subjects.—Two of us (D. M. P. and C. S. L.) and 2 medical students (G. G. and G. M.), all of whom had had experience in surgical scrubbing, were the subjects. Practice in the method and careful attention to details are necessary. The time allowed for scrubbing the palms and nails must be similar, since the count in these areas is so high as to make variations in technic immediately apparent in the final curve. The same brush was used throughout a series of scrubbings. Care must be taken to prevent loss of rinsings by splashing or allowing the elbows to drip outside the pan.

Cultures.—Making of Cultures: A 1 cc. sample of the fluid from each basin was taken with a pipet and placed in the center of a Petri dish. Bacterial infusion agar, with a p_H of 7.4, at 45 C., was poured into the dish, and the contents mixed by tilting. The plates were then incubated at 37 C. for forty-eight hours, and the colonies were counted. The cultures were made immediately after each scrubbing.

Counting of Colonies: A Quebec colony counter was used, and all colonies were counted. Occasionally, especially in the early basins, "spreaders" were encountered which made counting difficult, and such experiments were discarded. The size of colonies showed variation, and it seems improbable that every colony arose from a single bacterium. Small bits of stratum corneum which were washed off undoubtedly contained a number of bacteria, and these might have been counted as single colonies. The total bacteria of the hands and forearms, as determined by this method, would seem to be somewhat under the number actually present, but the same factor of error is present throughout the experiments and the results are comparable.

Computation of totals: The number of colonies counted for each plate was multiplied by 1,000 to obtain the figure for the total bacteria removed with each scrubbing. The amount of fluid in the soap solution used for scrubbing was disregarded. In over half the experiments the cumulative totals were plotted according to the method of Price, and the standard curve for each subject was determined. However, we have found the plotting of the actual bacteria removed in each basin, a method of expression used by Pohle and Stuart,[4] to be satisfactory. The curves herein given were obtained from an average of the results on at least 3 subjects unless otherwise stated.

Agents Studied.—Ointments: After three or seven minutes of scrubbing had been carried out, 5 Gm. of the ointment or sterile base was rubbed on each hand and forearm to the level of the elbow for approximately fifteen seconds and allowed to remain on the skin for three minutes, thirty minutes or one hour. Any excess of ointment was then gently rubbed off with a sterile towel and the series of scrubs resumed. Application of the ointment was ordinarily made after the seventh scrubbing, when most of the "transient" bacteria had been removed from the skin. Control experiments to determine the effect of using the ointment base without any antiseptic and of simply interrupting the series of scrubbings without

4. Pohle, W. D., and Stuart, L. S.: The Germicidal Action of Cleansing Agents: A Study of a Modification of Price's Procedure, J. Infect. Dis. **67**:275 (Nov.-Dec.) 1940.

application of ointment were made. The hands and forearms were ordinarily covered lightly with a sterile towel during the period of application of the ointment, but no significant differences were noted when the skin was exposed to the still air of a small laboratory room for similar periods. When the scrubbing was resumed after application of the ointment, when petrolatum or wool fat had been used a satisfactory lather could not be obtained with the initial basin. The lather in subsequent basins was satisfactory. The effects of the following ointments were studies: sterile petrolatum (white); sterile wool fat U. S. P.; sterile ointment U. S. P.; 3 and 5 per cent ammoniated mercury in petrolatum and emulsion [5] type bases containing a wetting agent, and 1:1,500 (0.06 per cent) phenylmercuric nitrate in ointment U. S. P. and emulsion [5] type bases.

Soaks: The hands and forearms were completely immersed in 8 liters of the solution for thirty minutes at 37 C. The effects of the following solutions were studied: sterile distilled water; 3 per cent aqueous solution of boric acid; 0.02 per cent potassium permanganate in water; 0.02 per cent potassium permanganate in water to which 0.1 per cent technical sodium lauryl sulfate (duponol) [6] or 0.1 per cent dioctyl ester of sodium sulfosuccinate (aerosol) [6] was added, and a 0.5 per cent solution of aluminum acetate.

Other Antiseptics: Sixty, 70 and 80 per cent alcohol (by weight) and Castellani's carbolfuchsin paint [6a] were studied.

Comment.—Price has made the following observations: (1) Ethyl alcohol in a strength of 70 per cent by weight is an extremely effective agent in producing "degermation" of the skin; (2) the commonly used mercurial compounds, when applied in aqueous solutions or tinctures, produce a sterile coagulum of the surface of the skin under which bacteria grow rapidly and hence, in terms of actual removal of bacteria from the skin, are not effective antiseptics; (3) the bacteria of the skin may be divided into transient and resident organisms; (4) the transient bacteria are easily removed from the skin by a variety of means, while (5) the resident bacteria are difficult to kill or remove; (6) under normal conditions the reestablishment of the bacterial flora of the skin after prolonged scrubbing requires approximately one week, but the wearing of wet rubber gloves accelerates this greatly, so that it may

5. Typical formulas were:

Petrolatum	34 per cent	Aerosol	2 per cent
Water	20 per cent	Liquid petrolatum	10 per cent
Aerosol	1 per cent	Glyceryl monostearate	12 per cent
Sperm oil	20 per cent	Carbitol	10 per cent
Glycerol monostearate	10 per cent	Spermaceti	7 per cent
Spermaceti	5 per cent	Water	59 per cent
Wool fat	10 per cent		

6. Duemling, W. W.: Wetting Agents, Arch. Dermat. & Syph. **43**:264 (Feb.) 1941.

6a. Castellani's paint is prepared as follows: Filter 10 cc. of saturated alcoholic solution of basic fuchsin and 100 cc. of a 5 per cent aqueous solution of phenol. Add 1 Gm. of boric acid. After two hours add 5 cc. of acetone, and after another two hours add 10 Gm. of resorcinol.

occur within a few hours; (7) pathogenic bacteria or fungi may suddenly become a part of the resident flora and persist for a long time. Price has reported numerous other observations of interest to dermatologists.[7]

The only other investigators who have thus far reported on experiments employing this method are Pohle and Stuart.[8] They confirmed Price's observation that a trained subject using a standard technic of scrubbing removes bacteria from the skin at a rate which is constant for the subject. They pointed out certain errors in technic which may produce variable results and modified Price's method of scrubbing in that no brush was used in washing the hands and the period of washing in each basin was prolonged to two minutes. They compared the relative germicidal activity of resin soaps and the usual commercial fatty acid soaps. They found that resin soap and commercial soaps containing a proportion of resin soaps were more effective in reducing the bacteria of the skin than the usual commercial fatty acid soap bars. In subjects who used a commercial soap containing resin soap daily for one week, substantial reduction in the bacteria of the hands was obtained. However, such soaps produced chapping of the hands.

RESULTS

The following data were obtained from a total of one hundred and ten scrubbing experiments by 4 subjects.

Average Normal Rate of Removal of Bacteria from the Skin.—In chart 1 is shown the average number of bacteria removed by successive scrubbings of the hands and forearms by 3 subjects according to the technic employed in these experiments. In the initial basin the bacterial count was over 2,750,000. In the first six basins the count falls rapidly; then the curve becomes less sharp and reaches a relative plateau at a level of somewhat above 250,000 organisms per basin. The total bacterial count of the hands and forearms varies widely, from 4,000,000 to over 40,000,000. When the total count is high, extremely large numbers of bacteria are removed during the first six to eight basins, and, as Price has pointed out, these are probably principally transient bacteria. We have attempted to determine some of the factors that cause increase or decrease in the total bacterial count of the same subject from week to week. Our data indicate that handling of the infected skin of patients

7. Price, P. B.: (*a*) Ethyl Alcohol as a Germicide, Arch. Surg. **38**:528 (March) 1939; (*b*) New Studies in Surgical Bacteriology and Surgical Technic, J. A. M. A. **111**:1993 (Nov. 26) 1938; (*c*) footnote 2.

8. Pohle, W. D., and Stuart, L. S.: The Germicidal Activity of Rosin Soap and Fatty-Acid Rosin Soap as Indicated by Hand-Washing Experiments, Oil & Soap **18**:2 (Jan.) 1941; footnote 4.

results in a high total bacterial count. Price has pointed out that the wearing of rubber gloves to the point of causing excessive perspiration causes the bacterial flora to rise. One of us maintained a high count during cold weather until the wearing of fur-lined gloves was discontinued. Lapses in scrupulous care of the nails are promptly reflected in the bacterial count. During these experiments one of us sustained a zosteriform herpes of the hand, and even after healing had occurred the total count remained at a high level for some time.

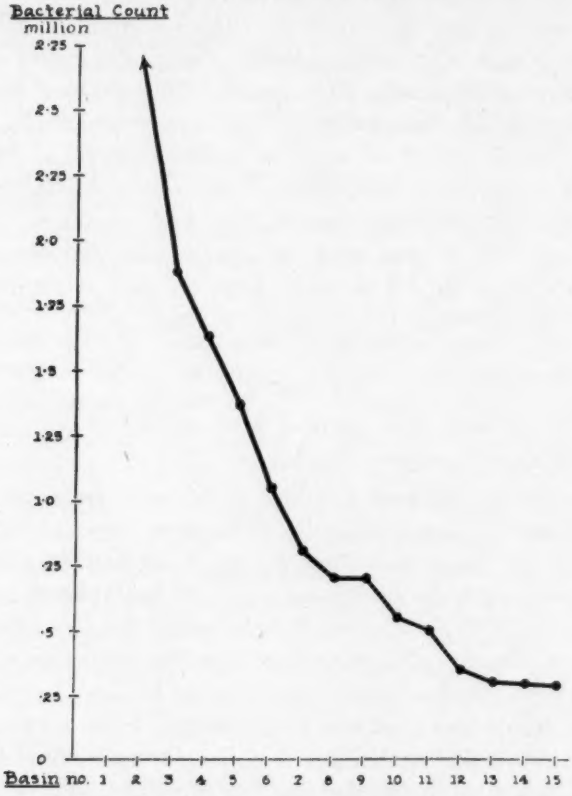

Chart 1.—The average number of bacteria removed by successive scrubbings of the hands and forearms (1.5 Gm. of soap in 4.5 cc. of solution for each arm) of 3 subjects.

Effect of Alcohol.—The effect of the application of 70 per cent alcohol by volume in reducing the bacteria of the skin is seen in chart 2. This was first pointed out by Price, and he stated that any marked deviation from this percentage markedly decreases the antiseptic effect. In our experience, 60 per cent alcohol by volume has a low antiseptic effect but 80 per cent or more by volume produces a satisfactory fall in the bac-

terial count. At Price's suggestion we attempted to treat several patients with superficial pyoderma with compresses of 70 per cent alcohol. The burning produced on abraded skin is so severe, however, that we have been unable to induce patients to persist with this treatment.

Effect of Castellani's Carbolfuchsin Paint.—An experiment with this compound was carried out in only 2 subjects, and in both the degerming effect was as good as that obtained with alcohol (chart 3). We have long used this solution for superficial pyodermic and fungous infections of the skin with satisfactory results. Since it is a complex solution, it is difficult to attribute the antiseptic effect to any single ingredient, but

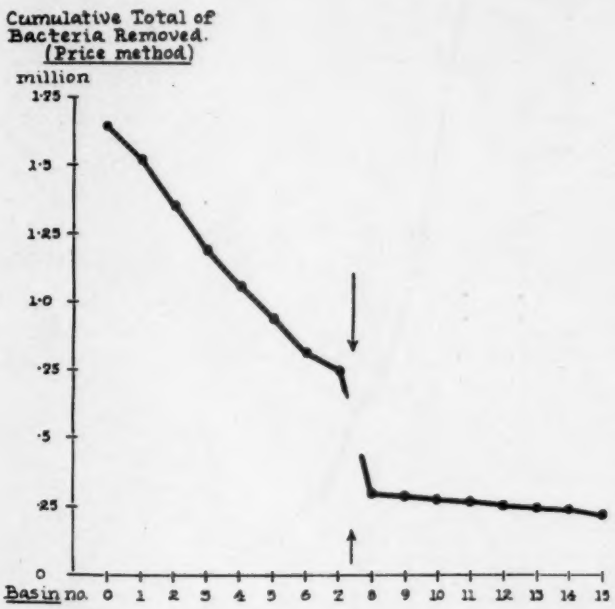

Chart 2.—The effect on the number of bacteria on the skin of the application of 70 per cent alcohol by volume. Arrows indicate the wiping of the skin with gauze soaked in the alcohol.

further study of it is being undertaken. It has the disadvantage of producing a prominent and persistent discoloration and occasional contact dermatitis.

Effect of Ointments.—In determining whether or not antiseptic ointments have a significant effect in lowering the bacterial flora of the skin, certain control experiments were necessary, including determination of (*a*) the effect of interrupting the series of scrubbings for varying periods without applying any ointment whatever (chart 4) and (*b*) the effect of applying a sterile ointment base for short periods (chart 5) and for

longer periods (chart 6). When the hands and forearms were exposed to the air for one hour, a moderate rise in the count of bacteria recovered in subsequent basins occurred. This rise is probably due to two factors, first, the softening effect of the previous scrubbing, with easier removal of the superficial layers of the stratum corneum when scrubbing was resumed, and, second, some actual increase of the bacterial flora by growth. The factor of air contamination does not seem to be important, since a rise was noted when the hands and forearms were loosely covered

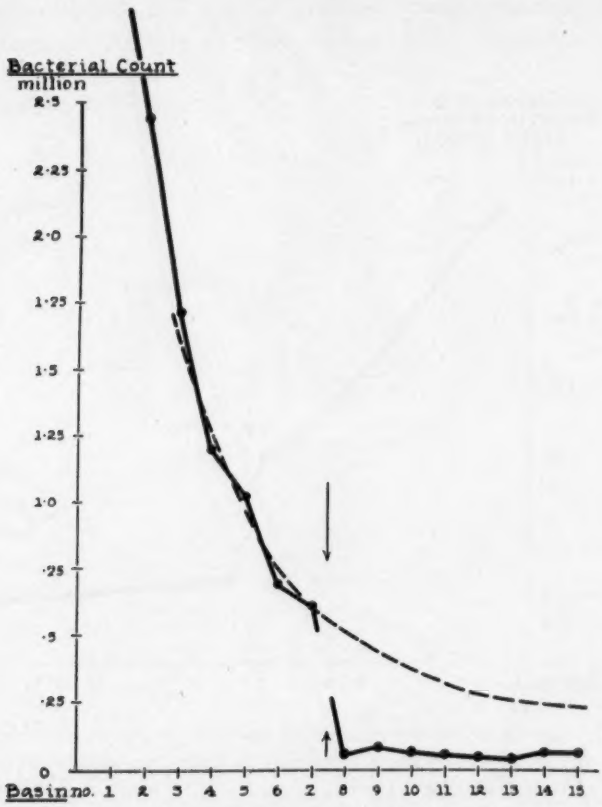

Chart 3.—The effect on the number of bacteria on the skin of the application of Castellani's carbolfuchsin paint (indicated by arrows) for thirty minutes. The dash line indicates the probable rate of removal without an antiseptic.

with a sterile towel. When a sterile ointment base was applied for two minutes and scrubbing was then resumed, a slight rise in the bacteria recovered was noted, which we believe must be attributed entirely to the softening detergent effect of the ointment and not to any bacterial regrowth. When an ointment base was applied for thirty minutes, a significant rise in the bacteria in subsequent scrubbings was noted.

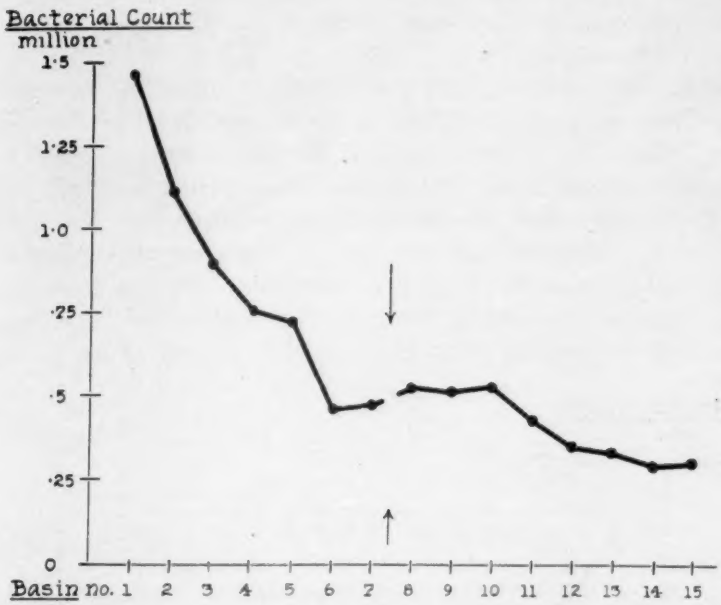

Chart 4.—The effect on the number of bacteria on the skin of interrupting the series of scrubbings for varying periods without applying any ointments. Arrows indicate exposure of the hands and forearms to the air for one hour.

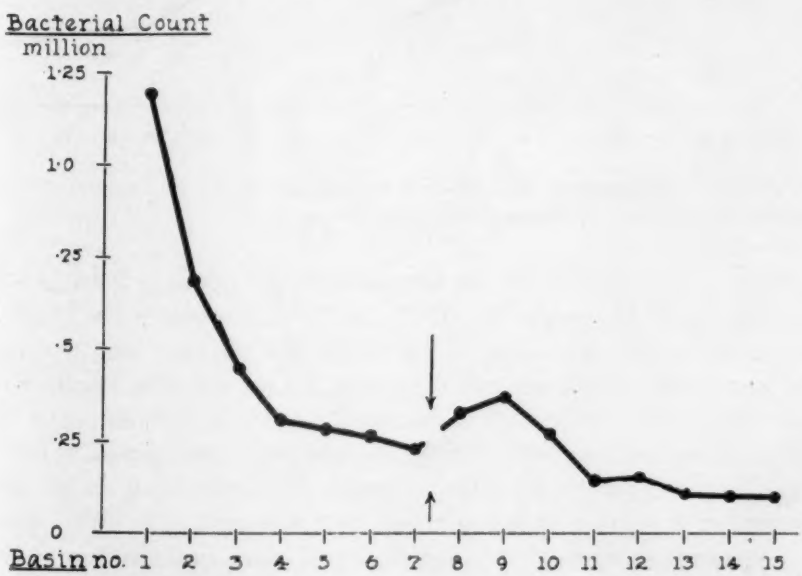

Chart 5.—The effect on the number of bacteria on the skin of the application of wool fat (indicated by arrows) for two minutes.

Again, we should attribute this to a combination of the softening effect of the ointment and to some bacterial growth under a relatively impermeable covering.

Ammoniated mercury and phenylmercuric nitrate in various bases have shown no decided antiseptic action as determined by this method. Chart 7 shows the average results of five experiments in which 3 or 5 per cent ammoniated mercury ointment was applied for thirty minutes during the period when the bacteria being removed from the skin were presumably principally transients. When these data are compared with the normal curve at this level, it is noted that there was some decrease in the bacteria recovered in the basin after application of the ointment, but not of the striking order seen with 70 per cent alcohol or carbol-

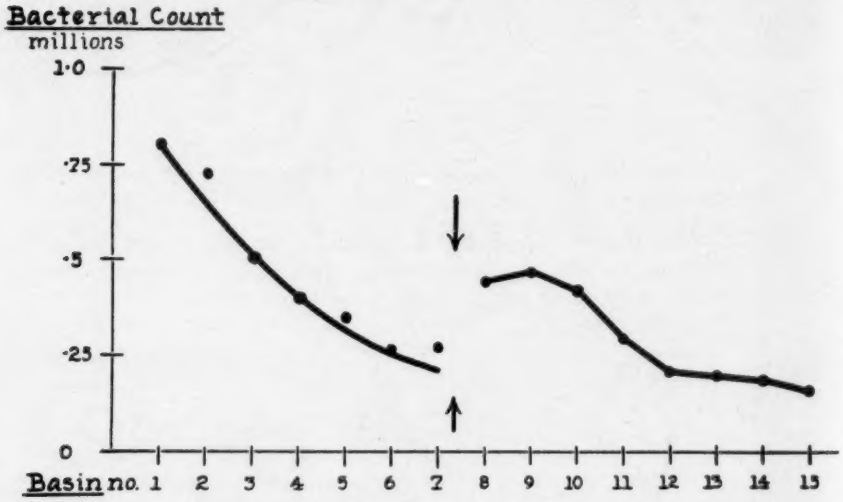

Chart 6.—The effect on the number of bacteria on the skin of the application of petrolatum (indicated by arrows) for thirty minutes.

fuchsin paint. When 5 per cent ammoniated mercury in petrolatum was applied for thirty minutes during the period of removal of the resident organisms, a rise was noted in one basin, but this was less than was the case when petrolatum was used alone (chart 8). The results with phenylmercuric nitrate, which has an excellent bactericidal effect on staphylococci in vitro, were similar to those with ammoniated mercury, whether a simple greasy base, a greasy base containing 1 per cent aerosol or a stearate vanishing cream base was used.

Effect of Compresses.—When the hands and forearms were soaked in sterile distilled water for thirty minutes at 37 C., a distinct rise in the number of bacteria recovered in several subsequent basins was noted

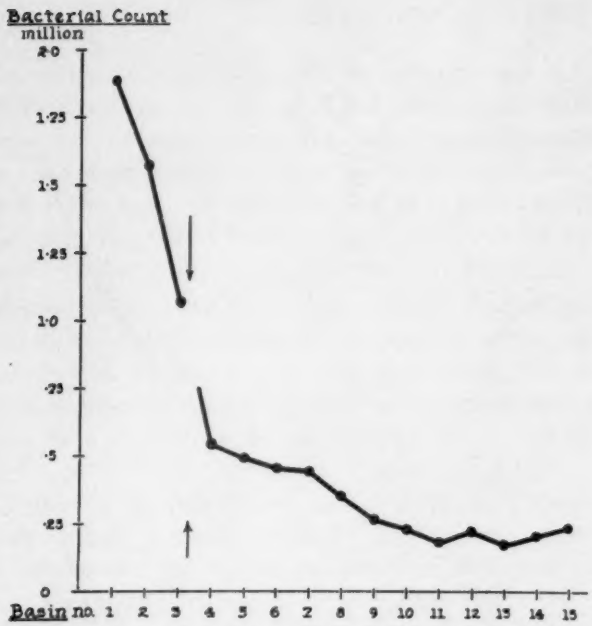

Chart 7.—The effect on the number of bacteria on the skin of the application of 3 or 5 per cent ammoniated mercury ointment (indicated by arrows) for thirty minutes during a period of removal of transient bacteria (average results of five experiments).

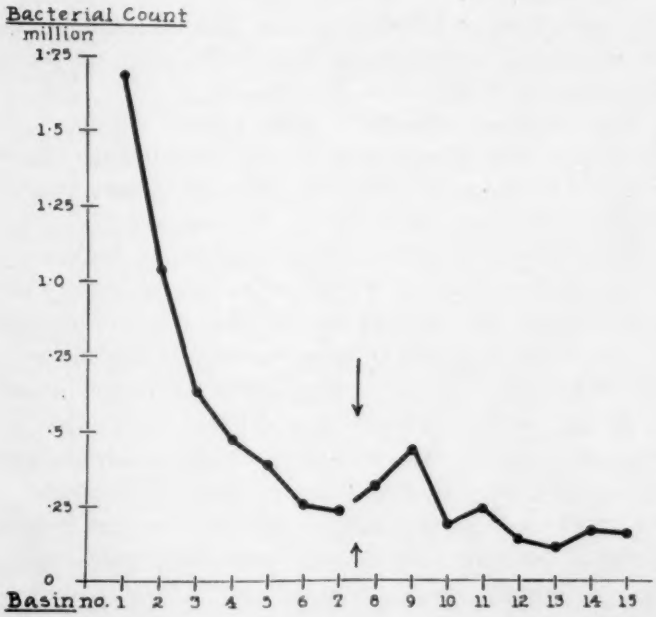

Chart 8.—The effect on the number of bacteria on the skin of the application of 5 per cent ammoniated mercury ointment (indicated by arrows) for thirty minutes (average of results in 2 subjects).

(chart 9). A similar effect was noted when 0.02 per cent potassium permanganate solution was used (chart 10), and no antiseptic action was noted after the addition of 0.1 per cent aerosol to the solution. When potassium permanganate or boric acid solution was used during the period of removal of transient bacteria, the expected curve was not greatly deviated from. A 0.5 per cent solution of aluminum acetate showed no significant antiseptic action.

Types of Bacteria Found on Normal Skin.—The bacteria removed from the skin of the various subjects showed decided similarity. Usually five different organisms were identified as present throughout the entire series of fifteen basins. Two had an orange pigment, two were white colonies and one a grayish white colony. All were gram-positive cocci occurring in irregular groups.

One orange-pigmented colony was hemolytic on blood agar, and the other was nonhemolytic. Neither liquefied gelatin. According to Bergey,[9] the hemolytic aureus strain would fall into the Staphylococcus group, though it differed from the classic Staph. aureus in that it did not liquefy gelatin and did not produce acid in mannitol. The result of a coagulase test was negative. The nonhemolytic aureus strain belonged to the Micrococcus group and reacted biochemically as Micrococcus luteus.

The two white colonies likewise showed a hemolytic and a nonhemolytic type. Neither liquefied gelatin. Biochemically the hemolytic organism resembled Staphylococcus epidermidis while the nonhemolytic organism resembled Micrococcus epidermidis.

The fifth organism, likewise a gram-positive coccus occurring in irregular groups, was a small flat grayish white colony which tended to spread. On biochemical testing the following results were obtained: litmus milk was acid and peptonized by the organism; it did not liquefy gelatin; it produced acid in dextrose sucrose, lactose, maltose, gelactose, dextrin and levulose but not in mannitol, salicin, xylose, sorbitol or dulcite; indole was not formed, and nitrites were not produced from nitrates. While the organism belonged to the Micrococcus group, it did not resemble biochemically any species under the Bergey classification.[9]

Aerobic and anaerobic blood agar cultures were made of several washings throughout the experiments; no obligate anaerobes were noted. No streptococci were recovered in any of these experiments.

Other types of bacteria identified infrequently were Sarcina lutea, the diphtheria bacillus (Corynebacterium) and gram-negative rods classified, respectively, as Escherichia and Bacillus pyocyaneus. In general, though the number of bacteria recovered in successive basins

9. Bergey, D. H., and others: Manual of Determinative Bacteriology, ed. 5, Baltimore, Williams & Wilkins Company, 1939, p. 261.

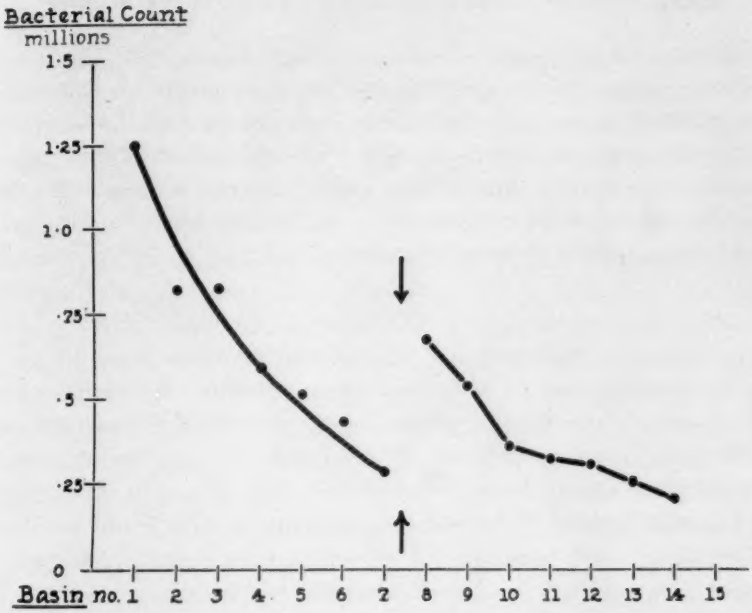

Chart 9.—The effect on the number of bacteria on the skin of soaking the hands and forearms (indicated by arrows) in sterile distilled water at 37 C. for thirty minutes.

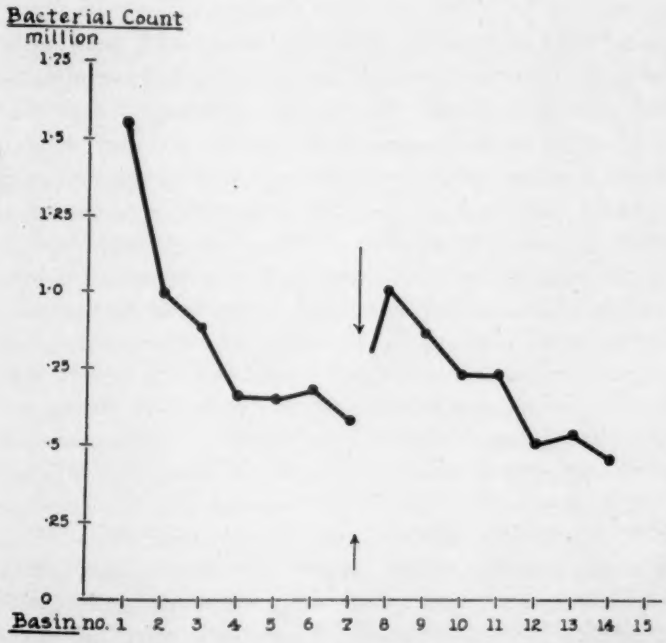

Chart 10.—The effect on the number of bacteria on the skin of soaking the hands and forearms (indicated by arrows) in 0.02 per cent potassium permanganate solution at 37 C. for thirty minutes.

was reduced by scrubbing or antiseptics, there was no significant change in the respective types. Qualitatively we were unable to differentiate between the transient and the resident bacterial flora on the basis of the types of bacteria recovered, though it should be noted that in most experiments a two or three minute period of prescrubbing was carried out. The study of the various types of bacteria recoverable from the normal human skin is being extended.

COMMENT

In evaluating these results, various considerations must be kept in mind, including caution in attempting to interpret the results of any single laboratory method in predicting the effectiveness of an antiseptic on the bacteria of superficially infected skin. Price's striking demonstration of the effectiveness of 70 per cent alcohol by weight in reducing the bacterial flora of the skin has been confirmed by Pohle and Stuart and ourselves. We have noted a decreased effectiveness of 60 per cent alcohol by weight in reducing the bacteria, but 80 per cent has shown a very satisfactory action in our hands. We doubt that extreme care in making solutions of alcohol for clinical use is necessary, so long as the percentage exceeds 70 per cent by volume (810 cc. of 95 per cent commercial alcohol diluted to 1,000 cc. at 25 C.).[7a]

Compound carbolfuchsin paint has shown a striking effect in reducing the bacterial flora of the skin. This is in accord with our clinical experience, and we have employed it with satisfactory results as both a bactericide and a fungicide. In vitro this compound does not show a decided effect on staphylococci. It is possible that the results of these experiments may be due to a coagulating effect on the surface produced by the phenol or resorcinol, and this compound is under further study in an effort to determine whether or not any single ingredient is responsible for the apparent antiseptic action. The application of the paint to hands and forearms is disfiguring and disagreeable for the subject, and this method is not practical for the study of antiseptic dye solutions.

Both ammoniated mercury and phenylmercuric nitrate ointment in various bases fail to show a decided antiseptic effect during the periods of application employed in these experiments. It is possible that during continuous applications of such ointment for days or weeks, significant reduction in the bacteria would be obtained; but at least these compounds are not rapidly effective, and clinically their action in controlling superficial infection is variable, in our experience. There is no indication from these experiments that the incorporation of emulsifying or wetting agents greatly increases the antiseptic effect of the mercurial compound, but such bases have practical advantages in a lessened

tendency to form an impermeable coating over the surface, in easy washability and promotion of removal of infected debris and in a tendency to absorb serous and purulent secretions.

It is noted that in general after the application of ointment bases alone the bacteria recovered in several subsequent basins often show an increase. We believe this is due to a combination of bacterial growth, the emollient effect of the ointment and subsequent removal of stratum corneum to which bacteria are adherent, but it is difficult to state which effect is predominant in increasing the number of bacteria washed off. It would seem that both possibilities are of clinical significance. For instance, we have observed cases of superficial impetiginous infections in which the infection seemed to spread rapidly under the applied ointment with apparent interference with removal of the superficial seropurulent material, especially when petrolatum is used as a base. On the other hand, if such processes are thoroughly washed with soap and water, the ointment may assist and increase the removal of infective micro-organisms through emollient action.

In so far as the results of these experiments indicate, commonly used compress solutions, such as potassium permanganate, boric acid and solution of aluminum acetate, assist in removing bacteria by their softening effect on the skin but do not exert significant antiseptic effect in the sense of killing bacteria.

It is possible that the results of experiments in which the effect of antiseptics on the normal bacterial flora of the skin is studied should not be used as a basis for determining the probable action of the antiseptic on pathologic bacteria. In superficial infections, such as impetigo, the organisms are part of the transient bacterial population, but in many dermatoses in which infection plays a role, the pathologic bacteria become extremely persistent members of the resident population. Thus far our experience with this method would indicate that the results are in good general accord with the final but often uncontrollable experiment of clinical experience and that it is useful as a single means of study.

In the treatment of any superficial pyococcic infection of the skin, cure is accomplished by (*a*) removal or killing of the responsible micro-organisms responsible or contributory to the process and (*b*) control of collateral local or general factors which decrease resistance of the skin against the infection or increase its reactivity to bacteria. Many of the problems relating to each of these are unsolved. Price has suggested the term degerming as best descriptive of the various methods of reducing the bacterial inhabitants of the skin in surgical antisepsis, and we believe that this concept is useful in considering the aims of treatment of superficial dermatologic infections.

Disregarding the important collateral factors relating to local and general resistance and reactivity of the skin against infection, we have outlined briefly what are believed to be the important means of reducing the bacteria responsible for a superficial infection and some of the reasons for failures in treatment. These are given as follows:

1. Ineffective bactericidal or bacteriostatic agents. It is evident on clinical experience that no single completely satisfactory antiseptic for the common superficial staphylococcic or streptococcic infections of the skin is available. We have seen numerous examples of the failure of all the commonly used antiseptics to control impetigo with the rapidity which might be expected of a really efficient bactericidal agent. It is believed that these failures may be attributed to several factors, including:
   - A. Ineffectiveness of the particular antiseptic even on close contact with the responsible bacteria or
   - B. Failure of the antiseptic to achieve contact in sufficient concentration with the site of infection, due to
     - (1) Application in an all grease base
     - (2) Favoring of bacterial growth by covering the infected site with a relatively impermeable grease film or a sterile coagulum under which bacteria grow freely, such as that shown to be produced by inorganic mercurial salts in aqueous solution [7b] or by calcium soaps [3]
     - (3) Application of the antiseptic on top of crusts or heaped-up debris
2. Failure to employ mechanical "degerming" methods, such as repeated vigorous washing with soap and water
3. Failure to employ surgical methods of drainage on even the smallest superficial pustules or follicules
4. Attempts to treat deep infections of the skin and subcutaneous tissues by antiseptics applied externally
5. Failure to recognize and analyze the complex local and general immune reactions influencing infections of the skin, the effects of disturbed vasomotor states and general underlying disturbances of metabolism.

SUMMARY

Mechanical cleansing of the skin is an effective means of reducing its bacterial inhabitants and is an important part of the treatment of any superficial pyogenic infection. In the strengths ordinarily used in wash-

ing, commercial fatty acid soap is not a good antiseptic, and the mechanical action of washing or scrubbing is most important in lowering the bacterial count. After the bacteria of the skin have been reduced there is a tendency for the flora to regain its previous level, and this rise may be increased by the wearing of gloves which cause sweating and prevent evaporation from the skin, by the handling of the skin of infected patients or by any focus of superficial infection in the region. It is probable that ointment bases, particularly petrolatum, increase the bacterial regrowth by acting as a relatively impermeable grease glove. However, if the skin is thoroughly washed after application of an ointment, it is probable that the removal of bacteria is facilitated by the grease, particularly when a base capable of emulsification is used.

In periods of application up to one hour, ammoniated mercury ointment and phenylmercuric nitrate ointments have no decided effect on the resident bacteria of the skin. It seems probable that longer periods of application are necessary and that mechanical removal of the ointment at intervals is a valuable part of producing the desired clinical effect. This is in accord with our clinical experience that mercurial ointments, regardless of the base used, are often relatively ineffective in the treatment of superficial pyogenic infections, especially if the ointment and debris are not removed by washing.

On the basis of these experiments, potassium permanganate, boric acid and solution of aluminum acetate all are relatively ineffective in reducing the bacteria of the normal skin. It is believed that these commonly used solutions act largely by softening the skin and products of superficial infection, thereby permitting easier removal of bacteria by washing or other means.

On the basis of qualitative bacterial studies, we are unable to distinguish between transient and resident bacteria of the skin. In the 4 subjects the types of bacteria removed in repeated experiments showed close similarity. At no time were streptococci recovered.

Alcohol in a dilution of 70 per cent by weight is an extremely effective agent in reducing the bacteria of the skin; percentages less than this are distinctly less effective. Unfortunately this agent is not of clinical value in the treatment of superficial pyogenic infections when abrasion of the skin is present, because of the extreme burning and pain produced by its application. Of the antiseptics studied, Castellani's carbolfuchsin paint was the only one which showed a striking antiseptic effect.

Wetting and emulsifying agents have shown no effect in increasing the antiseptic action of ammoniated mercury or phenylmercuric nitrate ointments or of potassium permanganate solution. However, it is

believed that these are of value in increasing the emollient action of substances applied to the skin and in assisting in the removal of grease and debris.

Dr. J. Harold Austin gave helpful criticism of this study.

ABSTRACT OF DISCUSSION

Dr. V. Pardo-Castello, Habana, Cuba: It seems to me that one must differentiate between the bactericidal and the bacteriostatic powers of locally applied drugs. I believe that a good many of our antiseptics function not by killing the bacteria on the surface of the skin but by stopping their growth and multiplication and allowing the defensive powers of the skin to act afterward.

I have been using lately, and with good clinical results, local applications of sulfanilamide and its derivatives. It seems to me that sulfanilamide, either in powder form or in ointment form, is one of the best local bacteriostatic drugs. I have been able to cure in forty-eight hours many recalcitrant pyodermas of the skin, such as impetigo of the bearded region in men. The application of full strength powdered sulfanilamide has proved a godsend in clearing up foul ulcers of the skin, for instance, neglected ulcers of the leg, granuloma inguinale and other secondary infections of the skin, in a short time, sometimes, I might say, in hours. At least in two or three days a decided reduction of the foul secretion is noted and, finally, practical disappearance.

Dr. James Herbert Mitchell, Chicago: I should like to ask, for my own information, if identification was made of the bacteria after the application of ammoniated mercury. Sabouraud many years ago showed that the follicular and glandular orifices have staphylococci as a natural inhabitant. It is impossible to get rid of them. It occurred to me that possibly the fats applied had dissolved the sebaceous material and had liberated the staphylococci in the orifices.

Also, I should like to ask if it is not possible that the production of a crust, such as is produced by gentian violet or by mercury bichloride, is not of some value in that it produces an anaerobic condition. Staphylococcus is an obligatory aerobe. Streptococcus can survive for seventeen hours, as shown by Sabouraud, if anaerobic conditions prevail. The fact that an artificial crust is produced may therefore be of some value.

Dr. Charles C. Dennie, Kansas City, Mo.: The authors have brought up the point of bacteriostatic action of certain substances. In pursuance of this investigation, for about a year my associates and I have been using sulfathiazole (2-[para-aminobenzenesulfonamido]-thiazole) in K-Y lubricating jelly for the treatment of infections of the skin, notably impetigo contagiosa. The sulfathiazole is incorporated in the jelly in a concentration of 3 to 5 per cent. The crust of the impetiginous lesion must first be removed by a dilution of clorox, whereupon the sulfathiazole is immediately applied and forms a crust. After three or four applications of this material the impetigo contagiosa is usually cleared up. We have also used sulfathiazole in powered sodium borate for fungous infections, especially when they are complicated by secondary infection, and believe that we have secured some good results. In the treatment of extensive burns, sulfathiazole has been used as a powder before the application of tannic acid mixture. In one case of extensive burns no secondary infection was apparent. However, sulfathiazole in powdered form will sometimes produce a severe conjunctivitis.

Dr. George M. MacKee, New York: My associates and I did some work along this line recently in attempting to obtain the flora from the average hand.

both the normal skin and slightly abnormal skin, not skin involved by real dermatitis but, say, slightly chapped skin. The flora did not vary much between the two types. We found in the flora an enormous number of nonpathogenic airborne organisms—saprophytes. We found, of course, the ordinary skin staphylococcus. I am speaking of the skin just of the hand, not of the face. Occasionally we found Staph. aureus and rarely Streptococcus. Then we did some work with various antiseptics. Our results were exactly the same as those obtained by Dr. Pillsbury. Seventy per cent alcohol we found to be the best agent. I was a little surprised to hear Dr. Pillsbury say that 70 per cent alcohol could not be used for purposes of treatment because it is too irritating. Perhaps I misunderstood him. We have not found it irritating either on patients or in the operating room, where all the surgeons use alcohol after scrubbing and before putting on rubber gloves.

Dr. Everett S. Lain, Oklahoma City: Since this most enlightening discussion of bactericidal agents used on the skin has drifted largely into giving clinical experiences with sulfanilamide, I cannot withstand the temptation to offer my experience with this drug. My associates and I have in private practice and also in our clinics been trying powdered sulfanilamide, incorporated in various ointments, including the wetting agents and others, for the past three or four years. For the past eighteen months we have been trying sulfanilamide powder dissolved in glycerin. I sent a clinical note to Dr. Fox for the Archives (Sulfanilamide in Glycerine in the Local Treatment for Pyodermas, Arch. Dermat. & Syph. **44**:257 [Aug.] 1941). Since January we have used this solution in many cases.

Briefly, after trying the various vehicles for sulfanilamide and determining that sulfanilamide is about 10 per cent soluble in warm glycerin, this preparation has become almost a routine treatment in all cases of localized pyodermic infection. Glycerin is a feeble germicide and possesses strong hydroscopic and antiphlogistic action on inflammatory tissue. It is also only mildly irritating even to raw tissue. The glycerin should be warmed; otherwise it does not take up the full 10 per cent (approximately 1 drachm [4 Gm.] of sulfanilamide to the ounce [30 cc.] of glycerin). We have now found it of some advantage to add as much as 2 drachms (8 Gm.) of the powdered sulfanilamide to the ounce of glycerin. As the glycerin is slowly absorbed, there remains a gumlike powder coating over the affected surfaces.

We have used this agent for nearly all of the various forms of pyoderma. It seems, however, to be of specific value for impetigo. After you have tried this remedy for localized staphylococcic and streptococcic infections, I think you will share my enthusiasm. I have found it more effective if applied in the form of wet dressings. The patients do not apply it well at home. When it is applied on the face of a child, it should be loosely bandaged for about twenty-four hours. The crusts usually adhere to the gauze and are painlessly removed with change of the first dressing. Impetigo is usually almost healed in three or four days. The preparation acts equally well in helping to clear and give a sterile appearance to any kind of a foul ulcer due to staphylococcus or streptococcus.

Dr. Donald M. Pillsbury, Philadelphia: This paper seems to have stimulated considerable comment on the local action of sulfanilamide and its derivatives. Drs. Wammock and Livingood and I have used a 5 per cent sulfathiazole ointment in about 75 cases of various superficial infections of the skin. Providing the proper type of base has been used, the results have been far better in the treatment of streptococcic and staphylococcic infections than those obtained with

the ordinary mercurial ointments and with some of the newer type preparations, particularly the quaternary ammonium compounds. From our results thus far, it would appear that a grease base is a much less effective means of applying sulfathiazole to the site of an infection than an oil in water emulsion type or vanishing cream type of base. So far we have encountered no evidence of absorption of sulfathiazole from such ointments, and the effect produced seems to be attributable entirely to the local action. We have also treated some patients with gramicidin.

In regard to irritation produced by 70 per cent alcohol, this occurs only when the continuity of the skin has been interrupted, and, unfortunately, the burning produced precludes the use of this for the treatment of most superficial infections. One extremely cooperative patient with sycosis barbae attempted to persist in treatment with alcohol compresses but was forced to discontinue it.

In our laboratory and clinical experience with the bacteriologic study of the skin, it is our feeling that too much emphasis has been placed on reduction in bacteria by killing by chemical means and too little on mechanical removal of the bacteria, whether by scrubbing, by emollient effect of ointments and compresses and by surgical debridement. The preventive effects of maintaining a reasonably low bacterial flora are, I believe, also of importance.

DIFFERENTIAL DIAGNOSIS OF PARAPSORIASIS

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Occasion may arise when nothing is more difficult in dermatology than a differentiation between parapsoriasis and allied conditions which are similar both clinically and histologically. About forty years has passed since Brocq united under the name "parapsoriasis" a group of diseases belonging to the class of chronic maculopapular, erythematous and scaly eruptions which have no effect on the general health and which last without benefit from treatment over a long period. These eruptions had been described by different observers in different countries. The same eruption has been given a variety of names, and in a great many instances the early stages of diseases well known at that time were confused with these new and less well known conditions.

The original clinical and histologic descriptions (even if under different and confusing names) pictured by the early students of this subject, such as Jadassohn,[1] Neisser,[2] Juliusberg,[3] Pinkus,[4] J. C. White,[5] Eudlitz[6] and Brocq,[7] were so complete that practically nothing new has been added. In 1910 Arndt[8] noted that melanoleukoderma on the shoulders and neck may be seen surrounding the individual elements of the eruption or that it may occur at the site of the eruption after its disappearance. The occurrence of leukoderma, which was thought

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1. Jadassohn, J.: Ueber ein eigenartiges psoriasiformes und lichenoides Exanthem, Verhandl. d. deutsch. dermat. Gesellsch. **4**:524, 1894.

2. Neisser, A.: Zur Frage der lichenoiden Eruptionen, Verhandl. d. deutsch. dermat. Gesellsch. **4**:495, 1894.

3. Juliusberg, F.: Die Parapsoriasis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 7, pt. 1, pp. 289-398.

4. Pinkus: Ein Fall von psoriasiformen und lichenoidem Exanthem, Arch. f. Dermat. u. Syph. **44**:77, 1898.

5. White, J. C.: A Case of Brocq's Erythrodermie Pityriasique en Plaques Disséminées, J. Cutan. & Genito-Urin. Dis. **18**:536, 1900.

6. Eudlitz: Psoriasis en gouttes d'aspect syphiloïde, Ann. de dermat. et syph. **132**:552, 1898.

7. Brocq, L.: Les érythrodermies pityriasiques en plaques disséminées, Rev. gén. de clin. et de thérap. **11**:577, 1897.

8. Arndt, G.: Ueber Brocqsche Krankheit nebst einigen Bemerkungen zur Frage der Parapsoriasis, Arch. f. Dermat. u. Syph. **100**:7, 1910.

at that time to appear only in syphilis and psoriasis, added another difficulty in differential diagnosis. In 1916 Mucha [9] and somewhat later Rusch,[10] Oppenheim [11] and Habermann [12] described an acute form of the guttate type which gave the clinical picture a more polymorphous character. With these two exceptions, nothing has been added to the knowledge of the disease from the clinical, histologic or etiologic points of view which might aid one in making a definite diagnosis. However, studies at a later date by Arndt,[8] Civatte,[13] Juliusberg,[3] Ormsby,[14] Wise,[15] Stokes,[16] Robinson,[17] Keil [18] and McCarthy [19] have clarified the picture considerably, and a number of conditions which were originally thought to be part of the group of parapsoriases can be ruled out.

One can be certain of only two well defined types of parapsoriasis: the guttate (or papular) type and the plaque or patch type. The third type, originally called parapsoriasis lichenoides by Brocq [20] and thought by him to be identical with parakeratosis variegata of Unna, Santi and Pollitzer and lichen variegatus of early English and American writers, has proved, at least in my opinion, to be an earlier stage or an atypical manifestation of mycosis fungoides, generalized lichen planus, acrodermatitis chronica atrophicans, poikiloderma and especially the other two types of parapsoriasis. The belief that parapsoriasis lichenoides might be a transitional stage between the guttate and the plaque type has been entirely abandoned. Tuberculosis, as suggested by Civatte,[13] has no place in the consideration of these eruptions.

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9. Mucha, V.: Ueber einem der Parakeratosis variegata nahestehenden Fall, Arch. f. Dermat. u. Syph. **123**:586, 1916.

10. Rusch: Pityriasis lichenoides chronica, Arch. f. Dermat. u. Syph. **125**:175, 1918.

11. Oppenheim, M.: Pityriasis lichenoides chronica mit varicellaartigen Vorstadium, Zentralbl. f. Haut- u. Geschlechtskr. **1**:107, 1921.

12. Habermann, R.: Ueber die akut verlaufende, nekrotisierende Unterart der Pityriasis lichenoides, Dermat. Ztschr. **45**:42, 1925.

13. Civatte, A.: (*a*) Les parapsoriasis de Brocq, Paris, Octave Doin, 1906; (*b*) Les parapsoriasis, in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 7, pp. 686-723.

14. Ormsby, O. S.: Parapsoriasis (Type Pityriasis Lichenoides Chronica): Two Cases, J. Cutan. Dis. **33**:390, 1915.

15. Wise, F.: Pityriasis Lichenoides Chronica: A Clinical and Microscopic Study, J. A. M. A. **67**:159 (July 15) 1916.

16. Stokes, J. H.: Clinical and Experimental Observations on a Case of Pityriasis Lichenoides Chronica, J. Cutan. Dis. **34**:343, 1916.

17. Robinson, S. S.: Pityriasis Varioliformis Acuta, Arch. Dermat. & Syph. **36**:991 (Nov.) 1937.

18. Keil, H.: Parapsoriasis en Plaques Disséminées and Incipient Mycosis Fungoides, Arch. Dermat. & Syph. **37**:465 (March) 1938.

19. McCarthy, L.: Parapsoriasis, in Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931, p. 199.

20. Brocq, L.: Les parapsoriasis, Ann. de dermat. et syph. **3**:433, 1902.

A study has been made of microscopic preparations from numerous cases of lesions diagnosed as parapsoriasis clinically by a large number of competent dermatologists for the purpose of determining whether a typical histologic picture for the three types occurs regularly and how much importance can be attached to the histologic observations when one endeavors to make a differential diagnosis.

PARAPSORIASIS GUTTATA (PITYRIASIS LICHENOIDES CHRONICA)

In the large majority of cases this disease should be diagnosed easily from clinical observation alone if one considers the characteristic appearance of the eruption, composed of papular and squamous lesions with transitional stages of one form to the other, its distribution and profusion, its extreme chronicity and its lack of response to treatment. The complete or almost complete lack of itching and the fact that the eruption has no influence on the well-being of the patient, although it may last for a score of years, should complete the clinical identification of parapsoriasis guttata.

The histologic picture varies with the age and type of lesion examined. Most observers agree that a characteristic and typical picture, such as is seen for lichen planus, for example, does not exist for this disease. The changes are those seen in any low grade chronic inflammatory process limited to the epidermis and upper layers of the cutis. Hamilton Montgomery [21] stated: "I was disappointed in looking over the slides of 45 cases of parapsoriasis to see the indefiniteness of the histologic picture."

Papular lesions which show no scales clinically often disclose a well defined parakeratotic scale extending over the entire summit of the papule. It rests on an epidermis that shows signs of beginning acanthosis, as evidenced by prolongations of the interpapillary portions of the rete malpighii. The epidermis is edematous and beset with small numbers of migrating lymphocytes in localized areas. The edema of individual papillae is well defined, and the perivascular infiltrate here is extensive but not dense. Polymorphonuclear cells have been reported in small numbers by some observers. Civatte,[18] who expressed the opinion that this disease can be diagnosed by histologic study alone, stressed the absence of polymorphonuclear leukocytes and used this fact in differentiating psoriasis and parapsoriasis. Histiocytes are increased in number, and plasma cells have never been reported. A sprinkling of mast cells may often be seen in the areas of densest infiltrate. The connective and elastic tissues suffer little, if any, permanent damage.

In older papulosquamous lesions the degree of involvement is more advanced. The parakeratotic layer of horn is thicker on the edges of

21. Montgomery, H.: Personal communication to the author.

the lesions and often less developed in the center. In some lesions the epidermis is more acanthotic over its entire extent, while in others the acanthosis is marked only on its borders. The center of the papule is covered by a normal or slightly atrophic epithelium still showing elongated interpapillary rete cones.

In this stage the edematous saturation of the epidermis in localized areas gives the epithelial cells a more or less homogeneous appearance due to destruction of the cell boundaries. Small clefts appear between the cells, but no actual vesiculation is produced. In exceptionally well developed papules these changes may involve the entire extent of the lesion. The number of migrating cells is increased, but as a rule no large localized groups are found, as in psoriasis. Montgomery differed with this statement, since he has occasionally seen small microabscesses in the epidermis.

As the process regresses the parakeratotic scales dry out and exfoliate. The epithelium regenerates, with lessening of the edema, and the infiltrate almost disappears from the late squamous lesions.

Some factors will now be discussed which are helpful in differentiating guttate parapsoriasis from syphilis, tuberculosis, psoriasis guttata, parapsoriasis en plaques and lichen planus.

In view of the rarity of this disease and the prevalence of syphilis, which it may resemble to a great degree, the first thought will be that one is dealing with a papulosquamous manifestation of syphilis. Differences in color of the lesions are of little value in distinguishing the two diseases, as all shades of red from orange or brown-red to the typical ham red of syphilis can be seen in parapsoriasis. If, as happens not infrequently, the eruption of parapsoriasis involves the palms and soles, the likeness to syphilis may be greatly increased. This is particularly true of an acute form with pustular and necrotic lesions. If areas can be found showing the different stages of transition of one type of lesion into another, parapsoriasis will be the diagnosis. This diagnosis is strengthened by the absence of lesions of the mucous membranes, the absence of involvement of the lymph glands and the absence of general symptoms. The fact that the scales can be rather easily scratched away en masse, leaving behind a smooth shiny surface, has been mentioned by many observers as diagnostic of parapsoriasis. Syphilitic lesions always show signs of induration, but this is not to be depended on as a differential aid, for often the early papules of parapsoriasis are distinctly infiltrated. The next recourse is the laboratory. In syphilis the Wassermann reaction is always positive during this stage and the histologic picture is different. The infiltrate in syphilis is much more dense and extensive, forming a wedge with its base located just beneath the epidermis and its point extending well into the subcutis. The cells forming the infiltration are almost entirely of the plasma cell variety

with a sprinkling of polymorphonuclear leukocytes and lymphocytes. In parapsoriasis the infiltrate is usually only moderately dense or even scanty and lies close up under the epidermis in the papillary and to a less extent in the subpapillary layer of the cutis. The infiltrate is composed of lymphocytes, histiocytes and a few polymorphonuclear leukocytes. Plasma cells are conspicuous by their absence. The edema of the papillary bodies and the migration of cells into the lower layers of the epithelium are always greater in parapsoriasis of this type.

Civatte [13] has called attention to the facts that the lesions in parapsoriasis guttata may rarely be arranged in groups and that they may tend to heal with scars (a questionable observation), presenting a picture that imitates the tuberculids. The tuberculin reaction may be positive, but this is of no diagnostic significance unless there is a focal reaction in the lesions themselves. The negative results of animal inoculation and the fact that histologic examination of tissue from patients with parapsoriasis never shows any signs of true tuberculous changes will decide the question.

The similarity in names indicates that at times there may be some confusion between this type of parapsoriasis and psoriasis guttata. This is especially true if the eruption of parapsoriasis is unusually extensive and if the individual lesions are brighter red and less sharply defined than is ordinarily the case. The chief distinguishing factor is the character of the scale, which is always much less in amount than that seen in an equally well developed eruption of psoriasis. The scale is usually situated on the center of the lesion and is brownish gray rather than the silver gray of true psoriasis. When this scale is removed one never sees the typical bleeding points of psoriasis, although the exposed surface may appear velvety and slightly moist.

The distribution of the eruption may be of importance. While in psoriasis there is a predilection for the extensor surfaces of the extremities, the face and the scalp, these areas may be comparatively or entirely free in parapsoriasis. Parapsoriasis is probably more frequently seen on the palms and soles than is psoriasis, but this is not an important differential point. Confluence of individual lesions to form an annular or serpiginous configuration does not occur in parapsoriasis, while it is rather common in psoriasis. The nails are commonly involved in psoriasis, but this complication has never been reported, to the best of my knowledge, in parapsoriasis.

The histologic differentiation between these two diseases may not always be easy, for they both represent a low grade chronic inflammatory process usually limited to the upper portions of the skin. The difference in the degree of the development of the various factors is of most help. In psoriasis the parakeratotic scale usually extends in a wide continuous band over the entire lesion, while in parapsoriasis the

scale is not so wide and occurs only at intervals; in other words, the inflammatory process produces much greater structural changes in psoriasis than in parapsoriasis. This idea is strengthened by the finding of mitotic figures in the epithelium and thinning of the suprapapillary portions of the epidermis in psoriasis. The acanthosis resulting in the prolongation and widening of the interpapillary rete cones is greater in psoriasis. Migration of inflammatory cells and edematous saturation of the epithelium are always greater in psoriasis, resulting in the formation of the so-called Monro abscesses, which are rarely if ever seen in parapsoriasis. In parapsoriasis the pathologic changes in the epidermis occur in sharply defined areas. Civatte [13] laid great stress on the minute areas of edema separating the cells of the lower layers of the epidermis; in the spaces thus formed only a few wandering lymphocytes are found. The edema never is sufficient to produce true vesicles even of microscopic size, and leukocytes are rarely, if ever, found in the intercellular spaces. This combination is considered by Civatte [13] to be typical for parapsoriasis guttata and sufficient to make a definite diagnosis from the histologic preparation alone. Few investigators feel that this disease has a characteristic histologic picture. Many authors have reported the presence of polymorphonuclear leukocytes in varying numbers in parapsoriasis, and I feel that one can no longer depend on this single point to make a differentiation. A further helpful point, not to be depended on too much, is that although the capillaries in the edematous papillary bodies are dilated in both diseases, in psoriasis these vessels occur high up, just beneath the epidermis.

If clinical and histologic studies fail to help, the results of treatment should solve the problem. Psoriasis responds to roentgen rays and strong topical applications, and parapsoriasis does not. However, one should not forget that parapsoriasis may disappear spontaneously or after treatment at certain seasons of the year. Remissions and exacerbations are fairly common in parapsoriasis guttata as well as in psoriasis.

Clinically the guttate type of parapsoriasis should not be easily confused with the plaque type, especially if one is dealing with typical expressions of the two diseases. The course of the disease and the development of the morphologic elements of the eruptions are different. The plaque type begins at smooth or slightly scaly spots which gradually develop into plaques of various sizes with smooth or only slightly scaly surfaces. These plaques last without visible change for years with no tendency to disappear. The guttate type begins as smooth, slightly infiltrated small papules, which later become more infiltrated and then become covered with an easily detachable and evident mass of centrally located scales. Still later the lesions appear as flat-topped, scarcely elevated and lightly scaling spots. All stages between the three types described may be seen in the same patient. Although this eruption may

last for years, remissions and exacerbations are common in the guttate type, a factor that is completely absent in the plaque type.

Histologically both types represent the same form of low grade chronic inflammatory change limited to the upper portion of the cutis and the epidermis. As a rule, the changes are less extensive and confined to more sharply limited areas in the guttate type than in the plaque type. Scale formation is thicker and more parakeratotic in the guttate type and more continuous and less patchy in the plaque type. The scale in the plaque type usually shows few, if any, areas of parakeratosis. Occasional leukocytes may be found in the parakeratotic scales of the guttate type but not in the horny layer of the plaque type. The migration of cells through the epidermis and the spacing of the rete cells as the result of edematous saturation have always seemed to me to be about equal in the two types. In the cutis the edema is different in the two diseases. In the guttate type it is usually limited to papillary bodies and not all the papillae are involved. In the plaque type the edema extends in a wide continuous band involving the papillary and subpapillary layers and is sharply demarcated on its lower border. Gans laid great stress on this band of edema, but Montgomery stated that he had encountered few cases that showed this feature. I found it 82 times in 96 slides from characteristic cases of the plaque type. Of course the results obtained from histologic studies depend on the age of the lesion examined, and it is difficult to be certain that one is comparing lesions in the same stage of development in the two diseases. I am inclined to believe that the two types can be separated more easily by clinical than by histologic studies.

Lichen planus should not be easily confused with parapsoriasis guttata. The distribution of the eruption with involvement of the mucous membranes and the color, shape and method of development of the lesions should be sufficient to diagnose lichen planus. Itching is practically always present in lichen planus, but it is rarely disturbing in parapsoriasis. Response to treatment and the difference in the duration of the eruption vary for the two diseases. Histologically it should be impossible to confuse the two diseases, especially if one examines typical lesions of each.

PARAPSORIASIS VARIOLIFORMIS

In addition to the cases of typical parapsoriasis guttata, which runs a chronic course and is characterized by the usual papular, papulosquamous lesions, one not infrequently encounters cases in which the course of the disease is either acute or subacute with the production of lesions that are vesicular, bullous, hemorrhagic and even necrotic, in addition to the typical lesions. There is an intensely generalized eruption which covers the entire body in a relatively short time. It is most pronounced on the trunk and upper extremities. The lesions begin as

round, waxy, yellowish to reddish brown papules which vary in size from that of a pinhead to that of a split pea. Vesicles quickly appear on the summit of some of the papules, and bullae are formed by a coalescence of several minute vesicles. If the process is intensely acute, hemorrhagic and necrotic changes take place in the lesions. Pigmented and scarred remains of healed lesions may be seen intermingled with the newer ones. All stages of development and regression of the lesions may often be seen in the same patient. There may be a general glandular enlargement with a temperature of about 100 F. and general malaise in some instances.

Buschke [22] and somewhat later Gottron [23] reported cases in which the usual papules and macules become covered with vesicles in a few days. The action of the unknown toxin ceased abruptly, and the lesions healed in a few weeks, leaving behind only dark brown pigmented areas without actual scars.

Histologic studies disclose changes usually seen in any acutely fulminating inflammatory process involving the epidermis and the upper layers of the cutis. There are hypertrophy of the horny layer and acanthosis of the epidermis as a whole. The marked edema produces ballooning and hydropic degeneration of the rete cells resulting in large cavities divided by septums. The remains of numerous degenerated rete cells may be seen floating in these cavities. This edema is so great that the junction between epidermis and cutis is completely destroyed in many places. Large numbers of lymphocytes and polymorphonuclear leukocytes migrate through the epidermis. Masses of these same cells form considerable mantles of infiltration about dilated vessels in the papillary and subpapillary layers of the cutis. Lesions in the process of involution show an increased production of horn on their edges with formation of crusts in the center.

The clinical picture of this type of parapsoriasis may simulate varicella, variola or malignant syphilis. One should try to find typical lesions of parapsoriasis guttata and trace their development through the more acute stages. The evolution of the lesions resulting in such a polymorphous picture should rule out varicella and variola. These patients are never as toxic as those with variola of an equal intensity of involvement. Syphilis may have to be ruled out by the results of the Wassermann test and by biopsy, which reveals in syphilis a large mass of cells composed of plasma cells deep in the cutis and subcutis as well as in the superficial portions of the skin. The final diagnosis may rest on the finding of a typical papulosquamous lesion and its study under the microscope.

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22. Buschke: Parapsoriasis, Zentralbl. f. Haut- u. Geschlechtskr. **16**:518, 1925.

23. Gottron: Acute verlaufende Pityriasis lichenoides vesiculosa, Dermat. Ztschr. **50**:39, 1927.

PARAPSORIASIS EN PLAQUES

If difficulty in the recognition of parapsoriasis en plaques occurs, it should arise only in the earlier phases of the disease. I believe a careful consideration of the clinical picture will be of more value in making the diagnosis than will the histologic picture alone.

The course of the disease, which is always extremely chronic and extends over a period of years, follows a set pattern with little tendency to variation. In the typical case the eruption, beginning as a single lesion, gradually spreads in a relatively short time (weeks or months) until the areas of predilection are involved. The eruption then remains stationary for many years with little tendency to exacerbation or remission. An occasional observer has reported seasonal remissions or clearings of the skin after therapy, but such reports make one suspicious of an incorrect diagnosis. Occasionally a single lesion or a small group of lesions may remain localized in one area for years before the eruption extends to other parts of the body. Such cases may cause considerable difficulty in diagnosis, and the problem is solved only by the passage of time. Sex and age incidence have no noteworthy significance in the disease.

The character of the eruption varies little in the typical case. The elementary lesion is strictly monomorphous because the eruption is made up almost entirely of smooth or slightly scaly, superficial plaques whose size, form and color may vary greatly in different regions of the body. The evolution of these plaques into higher morphologic elements, such as papules, nodules or tumors, with infiltration, atrophy, erosion or ulceration does not take place in this disease. Eczematization with a tendency toward weeping or crust formation usually results from friction of clothing or as the result of therapeutic applications. The shape of each lesion is more or less regularly round or oval as a rule. It is not uncommon to find larger plaques with polycyclic borders due to coalescence of individual lesions. Lesions arranged in sequence to form columns or strands are also commonly seen, and for some authors they are characteristic. These columnar lesions usually run parallel to the ribs on the trunk and in the the direction of the long axis of the extremities. Just as in many chronic eruptions, the lesions have a tendency to clear in the middle as they enlarge, and finally ring-formed or horseshoe-shaped lesions are produced. While at first glance the individual elements of the eruption may appear to be sharply demarcated, closer inspection will prove that they gradually fade into the surrounding healthy skin. The size of the lesions may vary within extreme limits from 1 cm. in diameter to the size of a palm or, rarely, even larger. The color of the plaques varies from a bright lemon yellow or a café au lait color to rose red or deep red, while on the dependent portions of the extremities the plaques take on a blue-red hue. Owing to coales-

cence of individual lesions and encirclement of areas of normal skin, a spotted or speckled appearance may be produced. This tendency was so great in 1 case that Brocq [20] described the appearance of the eruption as like that of the skin of a leopard.

In the earlier days much was written about atrophic lesions in this disease. Rille [24] and his pupil Rausch [25] expressed the belief that parapsoriasis en plaques simply represented a localized form of idiopathic atrophy of the skin. Although it is incontestable that occasionally certain plaques after many years may show a slight degree of true atrophy, such as is seen in long-standing chronic inflammatory processes like psoriasis or lichen planus, it is generally believed that true atrophy is not a part of the picture of parapsoriasis en plaques. Patches which have a wrinkled, atrophic appearance have been known to clear up without leaving a trace of any pathologic alteration of the skin. Furthermore, these pseudoatrophic patches when examined under the microscope show no signs of atrophy; they reveal as much inflammatory infiltrate as the other patches do.

The appearance of the surface of the plaques deserves a special word of mention. The surface is either smooth and gleaming or rough and covered with fine transparent or gray-white dry scales. Usually these fine scales are rather adherent but if one succeeds in removing them one sees a completely dry, yellowish red or bluish red surface which bears no resemblance to the moist, glistening red surface studded with pinpoint-sized bleeding areas seen after the lightly attached scales of true psoriasis are removed. Small purpuric spots may be produced within the limits of the plaques in parapsoriasis if their surfaces are rubbed too briskly (Arndt [8]). In some regions of the body the surfaces of the lesions appear to fall in very shallow folds, producing a pseudopapular appearance when they meet the natural furrows of the skin at right angles. The phenomenon accounts for the superficial lichenification reported by some authors. Brocq [20] originally stated the belief that this psendolichenification represented a transition from the plaque type to the lichenoid type of parapsoriasis. Today few observers believe that such a transition takes place.

Exceptionally the surface of the lesions is covered with somewhat thicker scales which are slightly folded or torn along the lines of the natural furrows of the skin. This condition has been compared by Arndt [8] to the appearance of a patch of skin painted over lightly with collodion. These collodion-like plaques were considered as plaques of atrophic skin, but they have been found to disappear leaving no traces of permanent injury to the skin. When fresh lesions of this type are examined under the microscope, no traces of atrophy can be detected.

24. Rille: Circumscripte idiopathische Hautatropie, Wien. klin. Wchnschr. **15**: 878, 1902.

25. Rausch: Pityriasis maculosa chronica, Dermat. Ztschr. **10**:594, 1903.

HISTOLOGIC PICTURE

In the majority of cases of parapsoriasis en plaques, from an examination of slides alone, without any knowledge of the clinical findings, it is impossible to make a definite diagnosis. However, when the clinical picture is known a careful microscopic study will serve to distinguish parapsoriasis from closely similar diseases that show much better defined histologic changes.

The microscopic changes are usually more evident than the clinical picture would indicate. They are limited to the upper layers of the corium and the epidermis, and the picture is the one that any chronic inflammatory infiltration of a moderate degree would be expected to show.

The changes in the epidermis are less evident than those in the corium and are probably secondary to them. The horny layer, which is of such importance in differential diagnosis, varies with the individual case. It may be of normal or somewhat increased thickness and, contrary to what may be expected, is loosely attached. If parakeratosis is present, it appears only in the form of minute isolated foci just above the areas of greatest edema of the papillary layer. The keratohyaline layer is either weakly developed or absent. As a rule, there is little proliferation of the rete Malpighii; in fact, the rete is often atrophic and thinned to a few rows of cells. The rete pegs, with the exception of an occasional elongated narrow one, have been almost completely wiped out by edema. In the ordinary case with only a moderate amount of infiltrate in the cutis the border between epidermis and cutis is well preserved. In instances in which the infiltrate appears as a heavy dense band of cells it presses on the epidermis and invades it from place to place, thus destroying the normal cutoepidermal line. Isolated areas of localized edema of the lower portions of the epidermis can usually be found. This edema of the epidermis rarely amounts to complete saturation. It separates the rete cells and at times may be sufficient to produce clefts of considerable size or even vesicles of microscopic proportions. However, it should be remembered that vesiculation does not take place here to the same extent as in eczema. As a further sign of chronic inflammation one always finds a certain number of lymphocytes migrating through the epidermis, but one does not find the large collections of cells usually seen in psoriasis.

The papillary layer is always the seat of a well defined edema with dilated lymph spaces. Often this edema is sufficient to flatten the papillary bodies almost completely. This edema in the large majority of the cases I have studied extends in a wide continuous band, sharply limited on its lower border, through the papillary and subpapillary layers of the cutis. In the ordinary case a moderately thick infiltrate appears arranged in nodes and strands about the vessels of the papillary

and subpapillary layers only—in other words, the infiltrate is usually high up in the skin. Riecke [26] has reported 2 cases in which considerable lymphocytic infiltration was found deep down, just around the sweat glands. I have seen this only once. In a small percentage of the cases the infiltrate takes the form of a continuous narrow but rather dense band just beneath the epidermis. The infiltrate is made up of lymphocytes and histiocytes with a sprinkling of mast cells and polymorphonuclear cells. No plasma cells are found here, an important point of differentiation, as will be seen later. Mitotic figures are not increased in the epidermis, and they are relatively absent in the corium. The connective tissue and the elastic tissue appear to be pressed on mechanically, and the fibers are separated by the presence of the infiltrating cells. Where the infiltrate is very dense there may be some actual destruction of these tissues. In lesions that appear atrophic clinically one finds about the same amount of infiltrate and signs of no more atrophy or destruction of the supporting tissues than in the usual type of lesion.

The entire picture is a most uncharacteristic one and simply represents a moderate degree of chronic inflammation involving the upper layers of the skin. It is this banal appearance that helps to differentiate parapsoriasis en plaques from closely similar diseases which have a more characteristic histologic picture.

DIFFERENTIAL DIAGNOSIS

Certain diseases in different periods of evolution may be extremely difficult to differentiate from parapsoriasis en plaques. I shall discuss these difficulties with reference to seborrheic eczema, mycosis fungoides, parapsoriasis guttata, psoriasis, leukemia, acrodermatitis chronica atrophicans, pityriasis rosea and purpura annularis telangiectodes.

Seborrheic eczema, which has a predilection for the scalp, face, sternal and interscapular areas, axillas, groins and navel and gluteal folds and which has a tendency to form the typical configurate or circinate lesions characterized by a tendency toward weeping, vesiculation and the formation of greasy yellowish scales, will not cause any difficulty. The perifollicular papular type of seborrheic eczema involving the trunk, so commonly seen in overnourished persons of Irish descent, will cause little disturbance. However, there is a type of this disease which does not involve the so-called seborrheic regions of the body and which does not produce lesions characteristic enough to recognize at a glance. This type is characterized by a few or a large number of well defined plaques on the legs, arms and lower half of the trunk. The

26. Riecke, E.: Zur Kenntnis der Pityriasis lichenoides chronica, Arch. f. Dermat. u. Syph. **73**:205, 1907.

plaques are about the size of the palm or often larger; they vary in color from yellowish or yellowish brown to yellowish red, pale or deep red, and their surface is covered by a fine branlike scale. These areas may be so similar to the plaques of parapsoriasis that a differentiation may be almost impossible clinically. In seborrheic eczema the patches are more sharply outlined and feel thicker than do those of parapsoriasis. In the former the scales are more abundant, tend to have a yellowish tinge when seen by reflected light and are more easily scraped off than in the latter. When the scales are removed in parapsoriasis, the underlying surface appears reddish, smooth and dry with occasional punctiform purpuric spots, probably caused by friction. After the scales are removed in eczema small pinhead-sized depressed areas indicating superficial erosion can usually be seen, although the surface appears smooth and dry as a whole.

Microscopically the clinical differences are more pronounced. In seborrheic eczema the proliferation of the rete is greater, as evidenced by the production of elongated rete cones and the presence of large numbers of mitotic figures. The intercellular and intracellular edema and the migration of leukocytes are also greater as a rule. The edema usually reaches a stage at which spongiosis and true vesicle formation, even if microscopic in character, result. Parakeratosis extending over the entire extent of each lesion, with almost entire absence of a well defined horny layer, is the rule in seborrheic eczema, and these two conditions are just the reverse in the majority of cases of parapsoriasis en plaques. The character of the inflammatory changes in the cutis is less well developed in both diseases and is of no value in differential diagnosis.

To these clinical and histologic differences should be added the results of therapy. Seborrheic eczema should be favorably influenced by sulfur ointments and baths and changes in living routine, all of which are of no avail in parapsoriasis. Despite these apparent differences which should aid in differential diagnosis one will occasionally meet with a case which defies a proper identification. I have had such a case under observation for eleven years. Large palm-sized plaques with the characteristics described have remained unchanged on the extensor and flexor surfaces of the thighs and legs for this long period. Histologic and clinical observation eleven years ago led to a doubtful diagnosis of seborrheic eczema. A second biopsy, in 1940, showed the same picture, but the lesions have not responded to any form of therapy. The long duration without change in character and the lack of response to treatment make one feel that the diagnosis of seborrheic eczema is probably a mistake, after all.

The differentiation of certain cases of parapsoriasis en plaques from cases of early mycosis fungoides holds the greatest interest for most

readers. Recently an effort has been made to prove that this disease is really an early stage of mycosis fungoides. It is better either to admit that a mistake in diagnosis was originally made or to beg the question by saying that in certain cases of parapsoriasis en plaques it may be practically impossible to differentiate the lesions from exactly similar lesions of certain (early) stages of mycosis fungoides. This is further borne out by the fact that in only a small percentage of cases of a condition diagnosed as parapsoriasis en plaques true mycosis fungoides developed while a large number have been followed for twenty or even thirty years without any change in the lesions having taken place. Montgomery [21] stated that of all the cases of parapsoriasis observed at the Mayo Clinic since its founding, in only a very few was there a mistake in diagnosis and the disease ended as mycosis fungoides.

I shall mention a few facts which serve to separate the two diseases in the large majority of cases.

In mycosis the picture is more graphic and leaves a more definite impression on the mind of the examiner. The lesions are more sharply defined; although young, they appear to be slightly thickened by an underlying infiltration. The shape of the lesions is also important, and the lesions vary greatly in size. There is a definite tendency toward circular, semicircular or horseshoe-shaped formations, with grouping of the lesions rather than simply plaque formation. If plaque formation is evident in mycosis, one will always find a few of the other types of lesion present. Central healing with a tendency toward ring formation occurs as a rule in mycosis and only exceptionally in parapsoriasis. The patches or plaques in mycosis often have a puffed-up or hivelike appearance, which is completely lacking in parapsoriasis. As the lesions develop and when they become more infiltrated with a tendency to show secondary eczematous changes even in minute areas, there should no longer be any doubt that the condition is mycosis and not parapsoriasis. The differences in color of the lesions of the two diseases are of less value in diagnosis. As a rule the lesions tend to be yellowish or yellowish brown in mycosis and reddish yellow or bluish red in parapsoriasis. Probably the most important difference is the relative absence of itching in parapsoriasis and the presence of definite itching, usually detrimental to sleeping, in mycosis. A feeling of discomfort so often complained of in parapsoriasis should not be confused with the real itching of mycosis. The remissions and exacerbations occurring naturally or as the result of roentgen ray therapy in mycosis should be a great help in differentiating the diseases in the early stages.

A careful study of the histologic changes should serve to differentiate the two diseases in the large majority of the cases.

The epithelial changes in mycosis are greater in every respect than those in parapsoriasis. The proliferation of the rete cells with numerous

mitotic figures results in the production of longer and broader rete cones. The degree of edema both within and between the cells is much higher, with the production of numerous vesicles like those seen in eczema. The vesicles are often filled with leukocytes. These changes are the rule in mycosis and extend over the entire surface of the lesion, but they are the exception in parapsoriasis, and when they do occur they appear as small foci, few in number.

The composition of the infiltration occupying the papillary and upper layers of the corium in both diseases is much more important than its relative density or its degree of development. In parapsoriasis the infiltration is made up almost entirely of lymphocytes (both small and large) and proliferating connective tissue cells (histiocytes) with a sprinkling of mast cells. Mitotic figures are hard to demonstrate, and plasma cells are practically never seen. In direct contrast to this the infiltrate in mycosis is much more polymorphous and interesting. It is made up, in about even proportions, of polymorphonuclear leukocytes, single or multiple nucleated plasma cells, proliferating connective tissue cells, mast cells and lymphocytes. Eosinophils are usually seen even in the early stages in small numbers. Not uncommonly the typical, so-called "mycosis cell" will be found in plentiful numbers. Mitotic figures are easily seen, and one gets the impression of a rapidly progressive process that is not seen in parapsoriasis. Dilated lymph spaces and vessels in the upper part of the cutis and edema of the papillary bodies are much more evident than in parapsoriasis.

Except that both processes are extremely chronic there is little clinical similarity in parapsoriasis guttata and parapsoriasis en plaques, and difficulties in differentiating the two should scarcely ever occur. In fact, they are so dissimilar that it seems to be a mistake to place the two diseases in the same group. The papular type suggests papular and squamous syphilis or psoriasis, while the latter may be confused with pityriasis rosea, mycosis fungoides or seborrheic eczema. Surely no more dissimilar conditions could arise. While both diseases are extremely chronic, the guttate type is characterized by its tendency toward exacerbations and partial or complete remissions, especially in summer. Such is rarely the case in the plaque type. The evolution of the eruptions differs in the two diseases. In the guttate type in the same person different stages of development of the lesions are seen, varying from a slightly scaly or smooth macule to a smooth-surfaced, infiltrated papule or a papule that is covered with a small cap of grayish scales that can be easily removed. In the plaque type it is always the smooth or only slightly scaly spot that gradually develops into a large noninfiltrated shiny or slightly scaly plaque which may become as large as the palm. I have already discussed the histologic differences under the guttate type.

Confusion of psoriasis and parapsoriasis en plaques should hardly ever arise. The distribution of the eruptions, their morphology, method of evolution and response to treatment are entirely different. The ease with which the brighter, more silvery and much more abundant mass of scales can be removed from psoriatic lesions, leaving behind a deep red moist surface showing bleeding points, should be sufficient to make a diagnosis. Histologically the difference in the two diseases is just as great. In psoriasis the lesion is topped by a well defined and extensive wholly parakeratotic layer with only here and there traces of a thickened horny layer. Numerous collections of leukocytes (Monro abscesses) are the rule in this scale. The rete shows well defined intercellular and intracellular edema with marked downward proliferation of the rete cones, often showing lateral daughter cones in their lower thirds. There is the characteristic thinning of the suprapapillary portions of the rete resting on widely dilated vessels to explain the presence of the bleeding points when the silvery scales are removed by curetting. In addition, there is a well defined migration of leukocytes through the entire epithelium. In parapsoriasis parakeratosis is the exception and occurs only in small foci when present; the proliferation of the rete is much less, as is also the degree of edema, and the migration consists of lymphocytes rather than leukocytes. In fact, the epithelium is often atrophic and thinned over the center of the plaque of parapsoriasis. The edema of the papillae and the dilatation of the vessels with their adjacent mantles of round cells and histiocytes are less evident in parapsoriasis.

On rare occasions leukemia may manifest itself on the skin only by the presence of large, slightly elevated areas of erythema whose conformation closely resembles large plaques of parapsoriasis. If true leukemia already exists, the blood picture will make the diagnosis. If an aleukemic or subleukemic stage is present, it may be impossible to differentiate between the two conditions at that time. Histologically the infiltration in the two conditions may be identical, but there should be more edema and migration of cells in parapsoriasis. Both these factors hardly suffice for a differential diagnosis.

Occasionally one sees lesions in parapsoriasis en plaques that have a slightly wrinkled surface that some authors have considered atrophic in origin. The plaques then suggest the changes in acrodermatitis chronica atrophicans or in pityriasis rosea during the regressive stage. It is now generally agreed that the atrophic character is more apparent than real and that no permanent damage is done to the skin in these areas, which often clear up without leaving a trace of atrophy. If confusion arises regarding identification of a patch of localized acrodermatitis before the atrophy is fully established, the histologic changes should separate the two diseases. In acrodermatitis the infiltration extends from the uppermost layers of the papillary bodies through the midcutis

into the subcutis in the form of dense well defined nodules or strands of cells. The infiltrate is composed of large numbers of uninuclear or multinuclear plasma cells in some areas and nodes of mononuclear cells with a scattering of plasma cells in others. The dense infiltrate disrupts the connective tissue and elastic tissue and eventually leads to true atrophy. The lymph spaces and blood vessels are usually well dilated. In parapsoriasis only the uppermost layers of the skin are involved, the infiltrate is relatively scanty, changes in the connective and elastic tissue are not noticeable and above all plasma cells are conspicuous by their absence.

Lesions of pityriasis rosea undergoing involution, especially if unusually large and oval, may have a close similarity to the wrinkled pseudoatrophic appearance of plaques of a rapidly developing form of parapsoriasis en plaques. The distribution of the lesions, their form, color and extent may be so much alike that it is only the course of future developments that will make a diagnosis possible. The lesions of pityriasis rosea clear up rapidly without atrophy while those of parapsoriasis remain about stationary. The same difficulty may be encountered when these two conditions are studied microscopically. The slides may be remarkably alike, and one may not be certain which slide is parapsoriasis of this rapidly developing type and which is the regressive form of pityriasis rosea. Perhaps it is safe to say that the parakeratotic scale is more abundant and more extensive in pityriasis rosea. Also the edema of the rete and the migration of cells are greater. As a rule the rete appears to have undergone a greater degree of proliferation, and the vessels in the papillary layer are more widely dilated. All these differences are only relative and not too trustworthy. Cases will be encountered in which only the progress of the disease will finally make the diagnosis.

Although there should not be the slightest connection between parapsoriasis en plaques and purpura annularis telangiectodes, I should mention the fact that occasionally on the legs the typical plaques of the former may show punctiform purpuric spots, especially after an attempt to remove the surface scales. On the other hand, the lesions of purpura do not always tend to undergo involution in the center and form annular lesions. Large plaques with slight scaling and petechiae may result. In both diseases typical expressions of each eruption will be found over widespread areas on some other part of the body. It should be remembered that central involution with resulting ring formation is the rule in purpura and the great exception in parapsoriasis.

PARAPSORIASIS LICHENOIDES

This condition presents a most confused symptom complex, which has never been thoroughly studied. The conditions originally described

as parakeratosis variegata and lichen variegatus have proved for the most part to be true examples of mycosis fungoides, parapsoriasis en plaques or *en gouttes,* generalized lichen planus or poikiloderma atrophicans vasculare.

Civatte,[18] who has been a keen student of parapsoriasis for over thirty-five years, has stated the belief that parapsoriasis lichenoides is identical with lichen variegatus of the early English writers. In all that time he observed and studied only 2 cases of his own. The first case, from the study of which he portrayed a typical picture both clinically and histologically, was observed for eighteen years. At the end of this period the patient died covered with tumors which Civatte [13] stated "were similar to those seen in the terminal stages of mycosis fungoides, although there was less itching and necrosis." To add to the confusion, it may be noted that before this case fell into the hands of Civatte [13] it had already been diagnosed as one of poikiloderma atrophicans vasculare by one of Majocchi's pupils. The disease in his second case, observed only six years, finally "cleared up, like a parapsoriasis en plaques usually does, without leaving any traces on the skin in spite of the fact that the skin had a definitely atrophic aspect when the eruption was at its height." The histologic descriptions and illustrations of his parapsoriasis lichenoides appear to me to be identical with the changes seen in many cases of parapsoriasis en plaques. In illustrating the changes in his first case he presented a microscopic drawing entitled "parapsoriasis lichenoide transforming into mycosis fungoides."

Jamieson [27] reported a case as one of lichen variegatus only to have the patient die a few years later of a disease which had all the earmarks of mycosis fungoides. Gougerot [28] presented before the French Dermatological Society on June 21, 1934 2 cases of a condition as parapsoriasis lichenoides of six years' duration that terminated as typical mycosis fungoides.

Basing his conclusions on a single case of his own and on 2 cases of Unna, Santi and Pollitzer,[29] published in 1890, Civatte [13] described what he believed to be the true parakeratosis variegatus, which could possibly be a fourth form of parapsoriasis. None of these cases were followed to the end; so what the patients actually died of is not known. In the case presented in 1923 by MacLeod [30] as one of parakeratosis

27. Jamieson, A.: Three Cases for Diagnosis, Brit. J. Dermat. **10**:324, 1898.

28. Gougerot, H.: Parakératose variegata et mycosis fungoïde, Ann. de dermat. et syph. **37**:121, 1934.

29. Unna, P. G.; Santi, and Pollitzer, S.: Parakeratosis variegata, Monatsh. f. prakt. Dermat. **10**:404, 1890.

30. MacLeod, J. M. H.: Case of Parapsoriasis of Mixed Type, Proc. Roy. Soc. Med. (Sect. Dermat.) **20**:36, 1927.

variegatus the condition was not thought to be that disease by Pollitzer, and Wise considered it poikiloderma. Civatte's clinical and histologic description [18] of his case fits beautifully into the picture of parapsoriasis guttata in my opinion. In fact, further on in his discussion he admitted that perhaps Csillag [31] was correct in believing that parakeratosis variegata is really a form of or identical with parapsoriasis guttata.

It is curious to note that at present the diagnosis of parapsoriasis lichenoides or parakeratosis variegata is rarely made and that if made it is practically never proved or agreed on by a majority of the dermatologists studying the case. I remember distinctly a case in recent years which was diagnosed as one of the lichenoid rather than of the guttate type because of the reticular arrangement of the lesions and an apparent atrophy of certain regions. After two years the reticulation and pseudoatrophy completely disappeared and the case was recognized as one of typical parapsoriasis guttata.

After a careful study of the literature I am inclined to believe that the diagnoses lichen variegatus, parakeratosis variegata and parapsoriasis lichenoides were made in the early days, before the clinical pictures of parapsoriasis guttata and parapsoriasis en plaques, as well as lichen planus, poikiloderma and especially mycosis fungoides, were well enough known for dermatologists to realize under what different and atypical forms these diseases could appear. How many today have an exact conception of the clinical picture of parapsoriasis lichenoides as it was originally described? For my part, I do not admit the existence of the third or fourth type of parapsoriasis either from my own experience or from descriptions in the literature.

CONCLUSIONS

Although one cannot diagnose parapsoriasis guttata with certainty from the microscopic picture alone, careful histologic studies enable one to separate it from closely similar eruptions, such as certain forms of syphilis and tuberculosis and atypical forms of lichen planus and psoriasis, provided the clinical picture in each case is known. Conditions that have been rendered atypical by the addition of vesicular, pustular, purpuric or necrotic lesions present real difficulties in diagnosis unless one reexamines the patient and studies microscopically a typical lesion, which can be found in every case at some stage of the disease.

In the large majority of cases of parapsoriasis en plaques, from an examination of slides alone, without any knowledge of the clinical find-

31. Csillag, J.: Zur Identität der Parakeratosis variegata mit einigen anders benannten Krankheitsformen, Arch. f. Dermat. u. Syph. **76**:3, 1905.

ings, it is impossible to make a definite diagnosis. However, when the clinical picture is known, a careful microscopic study serves to differentiate parapsoriasis from closely similar diseases that show much better defined histologic changes.

In the majority of cases reported originally as instances of parakeratosis variegata or lichen variegatus, which Brocq [20] later classified as cases of parapsoriasis lichenoides, the condition has proved to be an earlier stage or an atypical form of some other well known disease, such as mycosis fungoides, lichen planus or parapsoriasis guttata. In my opinion the clinical and histologic evidence offered in the literature is not sufficient to prove the existence of a third form of parapsoriasis.

In all cases of parapsoriasis, no matter what type is under consideration, the histologist will avoid many mistakes if he combines the knowledge gained from his microscopic studies with the important clinical facts, such as the character, duration and distribution of the eruption, the evolution of the individual lesions and their resistance to treatment.

The following dermatologists gave me permission to study slides from their collections: Drs. Andrews, Downing, Ebert, Eichenlaub, Ellis, Finnerud, Kanof, Kennedy, Ketron, Guy Lane, Machacek, Mitchell, H. Montgomery, Oliver, Ormsby, Pels, Robinson, Sandler and D. C. Smith.

ABSTRACT OF DISCUSSION

Dr. Fred D. Weidman, Philadelphia: It is indeed unusual to have the opportunity of studying so many sections from cases of a condition which has not afforded a great many biopsies. To illustrate, I have had some difficulty in locating material for a set of slides which is to be used in teaching at the next meeting of the American Academy of Dermatology and Syphilology, and parapsorasis was one of the stumbling blocks. The problem lay in the selection of a specimen that was representative or, better, typical. Accordingly, it is a great comfort to discover what difficulty the very best histopathologists—Dr. McCarthy, Dr. Ketron and others in the Washington-Baltimore group—have had in establishing a picture that was really diagnostic. My feeling is that this can be done only occasionally and that in the large majority of cases the most that the histopathologist can do is to state that the picture is compatible with parapsoriasis. One will encounter a larger number of cases in which it can be said that the picture is compatible with parapsoriasis when the condition is the plaque type; that is, there is more in favor of the plaque type being diagnosed than the guttate.

This field in which Dr. McCarthy has been working brings up the question in general as to how far one might dare to go in making positive, unequivocal diagnoses simply from a histologic section. The histopathologist strives to go as far as he can to bring as much as he can to the clinician, but there are positive limitations. The limitations are even more severe in the histologic field than in the clinical, because the histologist does not have such diagnostic data as the distribution and the duration of the eruption. The point that I want to make is that the clinician must be tolerant indeed toward the histopathologist. He must not expect too much of him. He must not expect so much that perhaps the pathologist

will be tempted to err as he tries to see more than can possibly be seen in sections from these noncharacteristic, diffuse dermatitides. By all means must clinical notes be supplied that are cogent and may turn the tide for a baffled microscopist.

DR. FRANK J. EICHENLAUB, Washington, D. C.: So far as parapsoriasis is concerned, I have come to the conclusion that if I can find nothing in the microscopic section that enables me to make any diagnosis, the condition is most likely to be parapsoriasis.

DR. CLARK FINNERUD, Chicago: At the March 1941 meeting of the Chicago Dermatological Society Dr. Otto Foerster made a statement which I am sure many of you have heard or thought with regard to parapsoriasis, namely, that in cases in which there is considerable question about the diagnosis, the most diagnostic thing about the condition histologically is the absence of diagnostic observations. That is approximately what Dr. Weidman and Dr. Eichenlaub have stated, and it certainly is true. Here is a definite cutaneous disease. One would naturally think that a histopathologist, just glancing through the microscope, almost instantly would be able to make an accurate diagnosis, but such is not the fact.

I am sure others as well as myself cannot help but wonder at times, especially in instances of the large plaque type of parapsoriasis, whether the condition is an entity. There have been instances of clinically definite parapsoriasis of the large plaque type which develops eventually into one of the lymphoblastomas. Of course, at a later date, the differential diagnosis histologically is comparatively easy.

As Dr. McCarthy stated, in many instances the differential diagnosis is better made clinically than histologically. The superficial changes in the epidermis, when slight and particularly with low power magnification, may closely simulate the Monro abscesses of psoriasis. But I believe that practically always, or at least usually, under high power magnification one can demonstrate an absence of polymorphonuclear leukocytes in these areas.

DR. LEE MCCARTHY, Washington, D. C.: I certainly agree with Dr. Weidman that some clinicians try to get the histopathologists out on a limb and then saw it off, when the latter have to look at sections without knowing anything about the clinical picture. The purpose of this paper is to prove that there must be a union of the clinical picture and the histologic picture of this disease; otherwise many mistakes in diagnosis will be made.

I should like to mention also that there is a type of leukemia characterized by a large erythematous plaque that has a slightly elevated border which closely resembles an early plaque of parapsoriasis. If it occurs in the subleukemic or aleukemic stage, one cannot make a differential diagnosis from parapsoriasis clinically or histologically, since the changes in both diseases are similar in this stage. One must wait for further development of cutaneous and blood changes.

There should not be any difficulty in recognizing the difference between purpura annularis telangiectodes and parapsoriasis en plaques; but there are some cases of parapsoriasis in which purpuric spots are seen, and there are some cases of purpura annularis in which annular lesions are not formed. I believe that parapsoriasis lichenoides, which is the term used by Brocq for parapsoriasis variegata, and lichen variegatus are just terms that were used in the early days when everybody was enthusiastic about this subject and felt the necessity of reporting a new disease. These diseases represent, I believe, early stages of mycosis fungoides or the two other types of parapsoriasis, particularly the guttate type, or they are atypical forms of lichen planus, and especially generalized lichen planus. Civatte, who recognized a third type of parapsoriasis, based his conclusions on 2 cases. One

of these cases he followed eighteen years, and he said the patient died of tumors like those of mycosis fungoides, only with less necrosis. Jamieson reported on a patient who died in eleven years of mycosis fungoides. Gougerot,[28] in 1934, reported 2 cases that had been presented at the Saint Louis Clinic, Paris, France, as instances of parapsoriasis lichenoides for a number of years. In both cases death was due to mycosis fungoides.

Curiously, of the 87 sections I received for study, there was only 1 sent in from a case of parapsoriasis lichenoides with a question mark following the diagnosis.

How many dermatologists have a clear, concise opinion of the clinical appearance of parapsoriasis lichenoides? At meetings of dermatologic societies if a patient is presented with this diagnosis, how many agree with the diagnosis? I remember I followed in Washington, D. C., for about three years a case of the lichenoid type of parapsoriasis. The eruption disappeared completely at one time, only to return later as a typical example of the guttate type of parapsoriasis.

HISTOCHEMICAL OBSERVATIONS ON MELANIN PRODUCTION IN THE SKIN

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For a quarter of a century studies of the problem of human pigment have been dominated by the histochemical reaction of Bloch, the dopa reaction. The importance of this reaction lies in the apparently established fact that its production denotes for the cell in question (we here ignore nonspecific reactions seen in leukocytes and sweat gland parenchyma) the capacity to make physiologic melanin. This significance for this reaction has been achieved through an endless number of studies with both animal and human skin, revealing a positive correlation between positive dopa reactions and the recognized capacity of the reacting epidermal cells to form physiologic melanin. Even more convincing has been the stronger positive correlation between the negative dopa reactions and the failure through functional perversion and damage of identical sites of skin to form pigment as disclosed clinically and histologically.

While there has been this general acceptance of the dopa reaction as an indicator of the capacity to form melanin, its use as background for an adequate elucidation of the nature and the manner of formation of physiologic melanin has met with bitter opposition. The literature for and against has become voluminous (hundreds of man-years of work). Bloch has led the proponents and Meirowsky the opposition, and neither group has yet surrendered its position.

Strange as it may seem, the literature fails to reveal adequate studies calculated to establish acceptable controls over the technic used in the histochemical procedure of Bloch. We refer specifically to the possible influence on spontaneous pigment formation in epidermal cells when, in

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frozen sections hardened in solution of formaldehyde, they are submitted to incubation for three hours at 37 C. and higher. Meirowsky and others called attention to postmortem production of pigment in epidermal cells of the skin. Unfortunately, in all these experiments the exact technic of Bloch was studiously avoided, and the importance of working under controlled conditions with microtome sections of skin removed during life was therefore not discovered. Neither group apparently suspected the complete implications of these observations of postmortem pigmentation of skin taken for biopsy.

Frozen sections, hardened in a 10 per cent concentration of solution of formaldehyde U. S. P. (less than twenty-four hours), placed in open beakers containing 0.85 per cent sodium chloride solution and incubated at 37 C. and at 56 C. for three hours, show unequivocal effects in the production of pigment as compared with the observations on the pigment in the immediately adjacent sections not so incubated. The effect was greater at the higher temperature, most conspicuously in the basal layer, though the other cells of the rete up to the granular layer entered into the reaction. This reaction of pigment production was discontinuous; i. e., only some of the cells showed reactions. The increase of pigment in these epithelial cells on incubation consisted both of more pigment in cells containing it in the control section and of pigment de novo in cells newly reacting. The latter type was particularly noticeable in cells in the malpighian layer, especially those lining the hair follicles. The new pigment was identical in color and size of particle with that in the control section. Further comment on the location within the cell of these pigment granules formed by experimentally accelerated production will be given later.

The Bloch school had found it necessary to postulate the existence of pigment granules too small to be seen through the resolving powers of the pathologic microscope in order to explain many histochemical reactions in the production of pigment granules. They offered the hypothesis that these infinitely small granules of physiologic melanin supply a nidus about which a reaction condensate takes place, resulting in the formation of visible particles. The silver nitrate test for melanin is generally accepted as an example par excellence of this mechanism. No validity, however, can be given to this hypothesis of pigment visibility via accretions about a mother particle when the reagent is not known to produce visible particulate precipitates in the reaction mixture in question. Especially is this true when the change in the reaction is initiated simply by factors of temperature and time, as previously indicated. To argue otherwise is to beg the question, in that insistence on a possible mechanism of production not amenable to proof involves knowledge of the mechanism we are seeking to disclose. Unless otherwise proved, one

must accept the visible evidence of new and more pigment granules as the production of these particulate masses wholly out of previously undifferentiated cellular substance. Furthermore, since simple incubation of excised skin may cause increased production of pigment, histochemical technics (the dopa reaction included) based on the use of at least a three hour incubation time are subject to whatever criticism may be based on the fact that the incubation technic will spontaneously evoke formation of pigment.

Judgment as to what early changes take place in cell protoplasm after removal of tissue from the intact whole can be included safely in the term "protein denaturation." Such denaturation materially affects the enzymatic equilibrium of cells. This consideration suggested the introduction into the reaction system of the forceful protein denaturants potassium cyanide and sodium fluoride. One per cent solutions of these were used in place of physiologic solution of sodium chloride, and the aforementioned experiments were repeated. The revelation therefrom was clear and unequivocal: a production of pigment not only exceeding that found in the control but well in excess of what was produced on incubation in 0.85 per cent solution of sodium chloride. In the experiments reported later the incubation temperature was limited to 37 C.

The cytoplasmic poison potassium cyanide has been thoroughly probed by the enzyme chemist. Potassium cyanide is destructive of the primary respiratory enzymatic chain in cells, leaving an enzymatic equilibrium requiring a relatively greater anaerobic metabolism for what remains and, by the same token, making the active oxygen present more readily available to those secondary systems requiring atomic oxygen as an end acceptor. We undertook a further variation in procedure calculated to influence the available oxygen and carbon dioxide in the reaction mixture. These variations took two forms. In one procedure the reaction mixture was overlaid with liquid petrolatum, to exclude atmospheric gases during the incubation; and in the second, after the mixture was thus overlaid with liquid petrolatum expiratory air was blown through the mixture for a full minute to saturate the solution with oxygen and carbon dioxide. The introduction of these variations led to further increased production of pigment over that resulting from incubation in an open flask.

There was a consistent, though not necessarily invariable, relation in all these procedures, in their tendency to increase the production of pigment. Using the nonincubated frozen section as control and base line value, the procedures in order of ascending influence on pigment production were as follows: (1) in saline solution, (2) in saline solution under liquid petrolatum, (3) in potassium cyanide, (4) in sodium fluoride, (5) in saline solution under liquid petrolatum, with oxygen and carbon

dioxide saturation, (6) in potassium cyanide under liquid petrolatum, (7) in sodium fluoride under liquid petrolatum, (8) in potassium cyanide under liquid petrolatum, with oxygen and carbon dioxide saturation, and (9) in sodium fluoride under liquid petrolatum, with oxygen and carbon dioxide saturation.

It was definitely shown that coverage with liquid petrolatum and saturation with expired air heightened the provocative effect of the solutions used and that the maximum effect was achieved with the use of sodium fluoride.

Several experiments with a preliminary exposure of the sections for one minute in boiling water showed that this treatment did not inhibit the acceleration of pigment production as aforementioned. In one experiment with human skin, the sample was kept in the solution of formaldehyde for eight days, without suppression of further production of pigment.

In contrast with the effects of potassium cyanide and sodium fluoride is the influence of mercury bichloride. This protein denaturant used in 1 per cent strength, after the manner described previously for the incubation of frozen sections, failed regularly to provoke increased production of pigment. Indeed, it appeared on occasion to show a tendency to bleach the pigment already present. Lastly, the protoplasmic poison silver nitrate has long been used to reveal pigment. The accepted explanation of its action has been its reduction and precipitation as silver element or silver oxide by the pigment already present, with consequent disclosure of more and larger brownish black particles in cells accepted as capable of producing pigment or engulfing it. Our studies challenge the simplicity of this explanation, but we must leave for another presentation the evidence and a discussion thereof, with the categoric statement that silver nitrate may also serve to provoke pigment formation *de novo* as at least part of its action.

Catechol and catechol derivatives readily darken and precipitate as melanin in alkaline mediums. Obviously, the basicity of the environment in which these experiments with frozen sections were carried out is a factor of prime consideration. The solution of the problem of the formation of human pigment still requires more definite knowledge as to the part played by auto-oxidation as an essential operative factor in its production. Before the data on the basicity of the solutions used in our experiments are given, the following explanation should be clearly understood. Under the conditions of our experiments the reactions observed were carried out within intact cells. In the language of enzyme chemistry the enzyme systems and substrata were walled off within the cell from the fluid environment in which they were placed. In view of this circumstance, consideration must be given to the degree that the cellular

content, possessed of buffering salts and protein, may resist the influence on its p_H by the solution that bathes it. Attention may properly be called at this point to the inadequacy of information on the specific character and degrees of influence of external mediums on chemical changes of the "intact cell" and to the unsafe practice of drawing unqualified conclusions as to chemical processes within the intact cell from experiments on tissue juices or other comparable solutions.

The solutions used in the experiments thus far mentioned ranged from the strongly alkaline, p_H of over 10 for 1 per cent potassium cyanide and 1 per cent sodium fluorine, to the moderately acid (p_H 4.5), as found in the 0.85 per cent solution of sodium chloride after it was overlaid with oil and charged with expiratory air. This definitely established the fact that the hydrogen ion concentration of the surrounding fluid medium in these experiments was not a determining factor in the reaction of increased production of pigment. But since provocation of pigment was greatest with the more alkaline solutions (potassium cyanide and sodium fluoride), it was yet to be established whether this alkalinity was the essential or merely a contributory factor under the conditions of our experiments.

To answer this question, experiments were carried out with phosphate buffer solutions with a p_H of approximately 5, 6, 7, 8 and 9 as the mediums for incubating the biopsy sections. The results were clear. The greatest increase in production of pigment came with the use of solutions with a p_H of 8 and 9. These observations spoke for autooxidation as the mechanism of the production of the new pigment, although it is to be emphasized that no facts are available as to the degree of change in the intracellar acid-base equilibrium effected by the use of these various buffers as enveloping mediums. However, these observations required further variation in our experiments to determine if the effects induced by the enzymatic poisons, potassium cyanide and sodium fluoride, were really due to enzymatic inhibitions and not secured through the strong alkalinity of their solutions. Furthermore, enzymatic poisons can be relied on to work in much smaller concentrations than 1 per cent, although here, too, it would be unsafe to be guided by what is known of these poisons as destroyers of enzymes in solution and in the presence of relatively little protein material. Nevertheless, experiments were made to elucidate this question. With the use of 0.1 per cent sodium fluoride and 0.1 per cent potassium cyanide, with phosphate buffer solutions at a p_H of 7 as diluents (final p_H about 7.2 to 7.5), our outlined procedures were repeated, and the results were carefully compared with the influence of the higher alkaline buffers (p_H 8 and 9) as used alone. The results were definite and unvarying. These enzymatic poisons in one tenth of the original concentrations and buffered to almost

neutrality induced decidedly greater increased formation of pigment than did the more alkaline buffer solutions alone. This speaks for enzyme catalysis as a genuine factor in the production of pigmentary increase in the epidermal cells of the skin.

Two of my collaborators, as experienced dermatohistologists, were charged with the duty of examining with me the several hundred sections of both human and guinea pig skin prepared in the study thus far, not alone to confirm the fact of increased production of pigment but to note the character and location of the product thus provoked. Our observations were as follows: 1. Whenever the control section showed the presence, however slight, of pigment granules somewhere in the epidermis—and this always included pigment in the basal layer though not necessarily limited to this layer—the procedures herein reported invariably operated to provoke new pigment. 2. The amount of pigment in the control sections did not serve as a measure of the degree of provocation effected. On the whole the less pigment present in the control, the relatively greater was the added amount experimentally induced. 3. Failure to provoke formation of new pigment occurred only in skin in which no pigment could be revealed in controls, if the skin was normal, although many sections containing no pigment in the control showed pigment on incubation. 4. Several specimens of pathologic skin revealed pigment in the control section without successful experimental increases. 5. The new pigment was deposited as particulate masses that tended first to locate at the periphery of the cell. In many instances these particles filled the entire cell, appearing then as a single homogeneous mass. When depositions were only at the periphery, the mass involved covered the complete range from a small arc of the circumference to all of the periphery of the cell. 6. At no time were dendritic cells revealed. Mention has already been made that cells up to the granular layer were involved in the reaction. 7. On occasion the experimental sections showed pigment in the chromatophores of the corium, whereas none was seen in the controls.

This introductory report on experimental studies of the physiologic changes of pigment permits of several impelling thoughts. Aside from the revelation of a practical procedure for the provocation in vitro of intracellular physiologic melanin, some light is thrown on the fundamental character of the mechanism of its production. The question of auto-oxidation versus enzyme catalysis find new support—at this point at least—for the operation of both principles. In behalf of an auto-oxidative process stand: (1) simple alkalinity of the environing mediums as a provocative circumstance, (2) the failure to destroy the potentiality for production of pigment by preliminary boiling in water of the sections for one minute and (3) the failure of the preliminary storage for eight

days of the sample of skin in a solution of formaldehyde to prevent the subsequent success in provoking new pigment. As supportive of the operation of an enzymatic catalytic mechanism stand: (1) the influence of three simple chemical compounds, strongly effective in disturbing the equilibrium of enzymatic systems, namely potassium cyanide, sodium fluoride and mercury bichloride, the first two to promote pigment formation and the third to inhibit it, and (2) the demonstration of optimum effects caused by these enzymatic poisons when they are buffered in slightly alkaline as against slightly acid mediums.

Further clarification is needed of the exact role which atomic oxygen plays in the production of melanin. Experiments are in progress seeking to throw more light on it. The procedures herein reported for the provocation of pigment production may readily lend themselves to an interpretation both simple and single: the conservation and direction of a minimal and rapidly disappearing supply of active oxygen to surviving enzymatic chains, one system of which concerns itself with melanin production. What needs to be emphasized is the fundamental fact that in vitro experiments with tissue sections represent studies with moribund cells. This bespeaks a rapid and progressive deterioration of the primary respiratory system, with the transfer of priority rights for active oxygen to secondary systems of which the melanin-forming function is one. It would appear that one is but seeking out by controlling conditions a rationalized explanation for postmortem pigmentation. There always remains the chasm to be bridged in understanding the pigmentary processes in the integrated skin. Sufficient for the moment is the thought that pigment-producing cells under the normal influences of integrated bodily function are kept in restraint by their own processes, processes readily labeled but vaguely understood, namely, integrated living processes.

We introduce this report with reference to Bloch's work and the dopa reaction. Indeed, we adopted his histochemical technic. Although in carrying out these experiments many "dopa reactions" were performed, it was not our intention at this time to use these data for a criticism of the value of this test or of the physiologic dicta underlying or derived from it.

We conclude this report with two factual statements concerning the dopa reaction: the first, that whenever a dopa reaction was positive we were always eminently successful in provoking formation of melanin by our procedures; the second, accepting the facts of the use of healthy sites of skin and the presence of pigment granules in the control section as evidence of the capacity to produce melanin, that our procedures invariably led to success in pigment formation, while the dopa reaction was positive, roughly speaking, in less than one third of the tests on the same samples.

ABSTRACT OF DISCUSSION

DR. SAMUEL M. PECK, New York: I wish to congratulate Dr. Sharlit because his fertile and inquiring mind has challenged the dopa theory, which apparently has been accepted by most dermatologists. The work of Bloch and his associates must be divided into two distinct phases: one in which the dopa reaction is used to indicate the presence of active melanoblasts, or active pigment formation, and one in which dopa is considered to be the propigment. I do not believe that the studies presented in any way controvert the validity of the dopa theory, which has been supported by the careful and painstaking work of many serious research workers. At the same time, these studies have in no way proved or disproved the question of the role of dioxyphenylalanine as the only propigment. What the authors seem to have accomplished is to demonstrate a nonspecific darkening of the epidermis in which the ordinary pigment formation, as I understand it, seems to play no role. Such apparent pigment formation has previously been demonstrated by Meirowsky (*Frankfurt. Ztschr. f. Path.* **2**:438, 1908) and by Miescher and Minder (1939). I do not believe that by the methods Dr. Sharlit and his collaborators have used or by their demonstration they have disproved the present concept of pigment formation as an enzymatic process. Probably by their method they have made visible the preformed pigment which was in fine colloidal suspension.

DR. SAMUEL W. BECKER, Chicago: I should like to support Dr. Peck's statement that the approach to the pigment problem must be from two viewpoints. The first is the specific formation of pigment, presumably from dioxyphenylalanine under the influence of an enzyme. It is supposed that melanoblasts, after having formed the pigment, transport the pigment granules to the epithelial cells. In the case of feathers, for instance, it is possible to see the pigment granules migrating from the melanoblasts into the feathers. The second phase of the pigment problem, and one with which Dr. Sharlit has dealt, has recently been studied in some detail by Miescher and Minder (Untersuchungen ueber die durch langwelliges Ultraviolet hervorgerufene Pigmentdunkelung, *Strahlentherapie* **66**:6-23, 1939), who showed that after pigment is present in an epithelial cell there are several different factors which may influence it. Dr. Sharlit and his collaborators showed that it may be oxidized. Reversing the process one may reduce it. I think it is in that field that these collaborators' work falls. I should like to ask whether they have ever seen this change in skin from a patch of vitiligo. There is no ferment reaction, and after the patch has been present for some time there is no melanin.

Rothman has shown that it is possible to produce pigment from tyrosine and that the first substance which is formed, as was shown by Raper some years ago, is dioxyphenylalanine. Vitamin C, for instance, will interfere with the oxidation of dioxyphenylalanine to melanin, but it does not interfere with the oxidation of tyrosine by tyrosinase.

While I was in Bloch's clinic I studied the effect of heat on tissue. I put sections of human prepuce, chosen because they were deeply pigmented, into an incubator at a moderate temperature. The chief observation was a tremendous shrinkage in the tissue. There was hyperpigmentation because there was concentration of melanin. The tissue was reduced to about one quarter of its previous length. Microscopic study of these sections did not reveal any particular difference in the number or shape of melanin granules.

I gathered from the presenters' explanation of the silver reaction that it is a reduction process. Miescher showed several years ago that when one mixes

melanin and silver two processes take place. The first is simply a darkening of preexisting melanin. Afterward there is a reduction of silver.

In demonstrating melanin, I use 2 per cent silver nitrate for only two hours. In other words, the process is halted by means of sodium thiosulfate before any appreciable reduction has taken place.

DR. GEORGE M. MACKEE, New York: The development of a practical technic for the provocation of physiologic melanin in epidermal cells should at least encourage a further study of fundamental concepts about melanin. The present report, which is the first of a series on this question, indicates an approach to pigment problems. The pigment formation produced experimentally by the use of destructive agents parallels, at least to some degree, clinical evidence of pigment response to cutaneous insult.

Postmortem pigmentation has embarrassed somewhat those who have accepted as final Bloch's theory of the melanin genesis. Bloch's theory still holds, but the work of Dr. Sharlit and his collaborators seems to show that knowledge of this subject is not yet complete. It is obvious that this work has an important bearing on the meaning of the dopa reaction. Presumably the authors will elaborate on this phase of the subject in future communications. It is a type of work that will have to be continued for a number of years.

DR. HERMAN SHARLIT, New York: I think it encouraging to find that without any attack on our part on the dopa reaction our presentation has evoked discussion that is chiefly a defense of this reaction. I was simply presenting facts. I have not made any pointed criticism of the dopa reaction at this time.

The melanin that is produced by incubating cutaneous tissue removed for biopsy is physiologic melanin and is new melanin within the meaning of my definition of "new." It is produced by the very technic that Bloch used when he added dioxyphenylalanine to the incubating solution to produce his reactions.

It would seem to me that after all these years of work with the dopa reaction, it should have been disclosed that incubation alone effects changes in the melanin-forming epidermal cell in the nature of provoked pigment formation. Particularly important was this revelation in the light of the insistence by adherents of the Bloch theory on explaining the reactions with the use of other melanin-forming compounds as simple oxidation condensation about microscopically invisible melanin already present. Now it is known that incubation itself causes the nidi of physiologic melanin about which any cotemporal precipitating reaction might condense; this is as true of the dopa reaction as of any other.

I might say that the dopa theory of melanin production cannot be overthrown by direct attack any more than it can be substantiated as yet by direct evidence. It will require, I imagine, the same type of circumstantial evidence to overthrow it as has thus far been offered to support it. One thing is certain: investigators cannot rest satisfied with the explanation of melanin formation via the dopa theory, even if it were true, because the explanation is inadequate; also there are many facts that challenge the adequacy and correctness of much of the evidence offered in its behalf.

COMPARISON OF FREI ANTIGENS

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The Frei test has been the subject of much discussion, and clinical studies tend to question its value in the diagnosis of lymphogranuloma venereum. On one hand there is evidence [1] to suggest that there may be false positive (cross) reactions in the presence of other venereal diseases. From another point of view, the value of the test in determining whether a given clinical lesion of one or another type is due to this disease is largely vitiated by the demonstrated fact that once infection has occurred, sensitivity of the skin (and a positive reaction to a Frei test) apparently persists for the remainder of the patient's life. These two considerations render the Frei test of limited diagnostic usefulness, at least in our hands.

Nevertheless, the test with one or another modification continues to be widely used. Practical difficulty in its application on a large scale has been generally encountered because of the scarcity of the antigenic material originally proposed by Frei [2] and employed by most investigators since Frei's publication, namely, diluted pus from an unruptured lymphogranulomatous bubo. The supply of this material has been limited to larger hospital centers and is often only intermittently available there, owing to the scarcity of freshly infected patients. Moreover, specimens of pus from different patients vary in antigenic content.

To meet these objections there was developed several years ago an antigen prepared from the brains of experimentally infected mice,[3] and

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Read before the Section on Dermatology and Syphilology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 4, 1941.

1. (*a*) Brandt, R., and Torpin, R.: The Dependability of the Skin Test in the Diagnosis of Lymphogranuloma Venereum and Chancroid, Especially in the Colored Race, Am. J. Syph., Gonor. & Ven. Dis. **24**:632-642 (Sept.) 1940. (*b*) Robinson, H. M.: Analysis of Intracutaneous Tests on Three Hundred and Nine Patients for Lymphogranuloma Venereum and Chancroid, South. M. J. **33**:144-154 (Feb.) 1940. (*c*) Beerman, H., and Ingraham, N. B., Jr.: Lymphogranuloma Venereum, Am. J. M. Sc. **197**:575-587 (April) 1939.

2. Frei, W.: Eine neue Hautreaktion bei Lymphogranuloma inguinale, Klin. Wchnschr. **4**:2148-2149 (Nov. 5) 1925.

3. Grace, A. W., and Suskind, F. H.: The Use of Standardized Mouse Brain Antigen for Performance of Frei Test for Lymphogranuloma Inguinale, J. A. M. A. **107**:1359-1365 (Oct. 24) 1936.

this substance was made commercially available. In the hands of various observers this antigen was found to parallel closely the results with bubo pus antigen in lymphogranulomatous patients and in supposedly normal controls. However, tests with the antigenic substance as well as control tests with normal mouse brain were observed to give nonspecific papular reactions in a high proportion of both normal and presumably infected persons, and these nonspecific reactions were often of such magnitude as to cause genuine confusion in interpretation.

To meet the objections to bubo pus antigens of scarcity and variability and to mouse brain antigens of nonspecific reactions, a new Frei antigen has recently been proposed.[4] This is prepared from virus grown in the yolk sac of living chick embryo, by a technic that was described as follows:

> Suspensions of virus-infected yolk sac . . . were inoculated into the yolk sac of eggs of 6 days' previous incubation. As soon as the embryos were moribund or dead the yolk sacs were collected, washed lightly to remove excess yolk and then weighed. They were ground thoroughly in a mortar with sterile quartz fragments and sufficient sterile physiological saline added to make a 10 per cent suspension. This suspension was centrifuged for 1 hour at 2,500 RPM in the cold and the sediment discarded. The supernatant was further centrifuged for 2 hours at 12,500 RPM in the cold. The resulting supernatant was discarded and the sediment resuspended in 0.1 per cent formalin-saline to a volume 20 times that of the original 10 per cent yolk sac suspension. Later, phenol to a final dilution of 0.25 per cent was also added. After 2 days the suspension was tested for bacteriologic sterility and for freedom from active virus by inoculation into the brains of mice and into the yolk sacs of developing hens' eggs.[4]

This yolk sac antigen is commercially available under the name of lygranum. Preliminary reports of its use have been published by Grace, Rake and Shaffer.[4] It is said to be more specific than mouse brain antigen and to provide fewer nonspecific reactions with control material containing no virus and prepared from normal yolk sac extract by the same process as lygranum itself.

PURPOSE OF THIS STUDY

Neglecting entirely both the important question of the occurrence of cross reactions in the presence of other venereal diseases and the confusion resulting from the known persistence of the Frei reaction after a subclinical or forgotten infection, we seek solely to compare the results obtained by intracutaneous testing with these two new products against the results obtained in the same group of patients with a battery of Frei (human bubo pus) antigens.

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4. Grace, A. W.; Rake, G., and Shaffer, M. F.: A New Material (Lygranum) for the Performance of the Frei Tests for Lymphogranuloma Venereum, Proc. Soc. Exper. Biol. & Med. **45**:259-363 (Oct.) 1940.

Several (usually three or four) antigens were prepared from human bubo pus by the usual technic.[5] These were employed in dilutions with physiologic solution of sodium chloride ranging from 1:2 to 1:10 after a trial of their potency on known reactors had revealed the optimum dilution. The dilution most commonly used was 1:5, but in cases in which large amounts of pus were obtained a dilution of 1:2 was found preferable. It has been noted many times that the smaller the amount of pus obtained from a bubo, the more potent the antigen it produces, and that the larger the amount, the weaker the antigen. Controls were not employed with bubo pus antigens.

The mouse brain antigen was the commercially available product.[6] Most patients tested with it were also tested with the control emulsion of normal mouse brain.

Lygranum (yolk sac antigen) [7] was likewise usually controlled with simultaneous intracutaneous injection of normal yolk sac extract.

NONSPECIFIC REACTIONS

Our experience agrees with that of all previous investigators as to the incidence of nonspecific reactions with the use of bubo pus and mouse brain antigens. With bubo pus antigen we and others have observed their incidence in about 30 per cent of patients tested; but the papules are small (rarely over 4 mm. in diameter), the zone of surrounding erythema is minimal or absent and vesiculation or ulceration is never present. These nonspecific papules are easily distinguished from true positive reactions.

When mouse brain antigen was used, we confirmed the statements of others [8] that in supposedly normal persons both the virus-containing antigen and the emulsion of normal mouse brain produce nonspecific papules in a high proportion (80 to 90 per cent) of persons tested. Moreover, these nonspecific papules may be of such a size (7.5 mm. or even larger) and degree of infiltration as to cause serious difficulty in differentiation from a true positive reaction.

Regarding lygranum, only one statement as to nonspecific reactions has so far appeared in the literature. Grace, Rake and Shaffer [4]

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5. Frei, W.: On the Skin Tests in Lymphogranuloma Inguinale, J. Invest. Dermat. **2**:119-124 (June) 1939.

6. This was supplied by the Lederle Laboratories, Inc., Pearl River, N. Y.

7. This was supplied by E. R. Squibb & Sons, New York.

8. (*a*) Strauss, M. J., and Howard, M. E.: The Frei Test for Lymphogranuloma Inguinale: Experiences with Antigens Made from Mouse Brain, J. A. M. A. **106**:517-520 (Feb. 15) 1936. (*b*) Binkley, G. W.; Love, W. R.; Schwartz, W. F.; Hitch, J. M., Jr., and Morgard, G. A.: Mouse Brain Lymphogranuloma Venereum Antigen: Clinical Experience at Cleveland City Hospital, Arch. Dermat. & Syph. **38**:383-388 (Sept.) 1938.

expressed the belief that with this substance, whether control or virus-containing extract, nonspecific papules appear only rarely. This has not been our experience, both in patients with lymphogranuloma venereum and in those supposedly free from the disease. In at least 70 per cent of those reacting to human bubo pus antigens who were tested with lygranum, the control substance caused an erythema from 5 mm. to 1 cm. in diameter and frequently also nonspecific papules from 1 to 3 mm. in diameter. These also occurred in nonreactors to human bubo pus (this reaction is not always easily seen in Negro patients). In white patients this nonspecific reaction may be so inflammatory (measuring up to 1 cm. in diameter) that, unless the physician performing the test is warned, interpretation is difficult. Cutaneous tests with lygranum extract and control were performed on 10 normal physicians, in 8 of whom there were erythema and papule formation, the erythema measuring from 5 mm. to 1.2 cm. in diameter and the papules from 2 to 4 mm. in diameter. In 2 of these persons the nonspecific reaction was equivalent to that observed with lygranum extract in known positive reactors to bubo pus antigen.

COMPARATIVE POTENCY OF REACTIONS IN POSITIVE REACTORS WITH THE THREE TYPES OF ANTIGENS

The size and infiltration of a papule or nodule with or without vesicle formation decide whether the reaction is negative or positive. As a rule, if the resulting papule or nodule is 5 mm. or over—and certainly if it measures 1 cm. or over—the reaction is termed positive. One of the reasons given for preferring mouse brain antigen is that this antigen may be standardized as to potency and that the degree of reaction on any one known reactor does not vary, even though specimens from several different lots are used. The same reason is given for the use of the yolk sac (lygranum) antigen.

In our hands the reaction produced by mouse brain antigen has almost always been larger and more infiltrated than that by yolk sac or bubo pus antigen. In a few instances (less than 1 per cent) the reaction to the mouse brain antigen was smaller than that caused by bubo pus antigen. In most of the tests the reaction to the yolk sac antigen was as large and infiltrated as that produced by the most potent or reactive bubo pus antigen in the series.

Vesiculation and ulceration occur most frequently with mouse brain antigen, slightly less so with yolk sac antigen and much less frequently with bubo pus antigen. In several patients, however, all three types of antigen caused bullous formation and ulceration. In all of these the nonspecific papules were insignificant, less than 5 mm. in diameter.

COMPARATIVE RESULTS OBTAINED

The results of simultaneous tests with human bubo pus and mouse brain antigens in 701 patients are presented in table 1. There was a high degree of correlation, identical results with the two antigens being obtained in 665 of the total 701 patients (94.8 per cent agreement). It is worth noting that 19 reactions were recorded as positive with mouse brain antigen but negative with human bubo pus, while in 18 the reverse was true. This is a direct expression of the difficulty of interpretation even by experienced persons of nonspecific reactions.

A similar comparison for human bubo pus and lygranum is shown in table 2. Here also there is close correlation, since the two tests agreed in 116 of 127 persons tested (91 per cent agreement). However,

TABLE 1.—*Reactions to Simultaneous Tests in Seven Hundred and One Patients*

Reaction to Human (Bubo Pus) Antigen	Reaction to Mouse Brain Antigen	
	Positive	Negative
Positive, 243	225	18
Negative, 458	19	439

TABLE 2.—*Reactions to Simultaneous Tests in Seven Hundred and One Patients*

Reaction to Human (Bubo Pus) Antigen	Reaction to Chick Embryo (Lygranum) Antigen	
	Positive	Negative
Positive, 58	51	7
Negative, 69	4	65

while the same difficulty in interpretation of nonspecific reactions was found in persons reacting to lygranum, it was also noted that the yolk sac antigen was apparently less potent than our best human bubo pus antigens, since in 7 persons with positive reactions to the latter, tests with lygranum gave negative results.

COMMENT

Besides diluents and preservatives, when they are used, human bubo pus antigen contains broken-down lymph node cellular material, pus, sometimes a little blood and the virus of lymphogranuloma venereum. Mouse brain antigen contains brain tissue rich in cellular elements, merest traces of blood, if any at all, and the virus. Yolk sac antigen is essentially free from cellular material, and the technic of its preparation is such that one may assume that it contains only certain proteins, fats and the virus.

It would seem clear, therefore, that since these three different antigens give such remarkably consistent results, they must contain in common an antigenic substance which is not directly dependent on its mode of derivation. The only factor which these equally reactive antigens have in common is the virus. This would suggest, therefore, that the virus itself provides the antigenic substance.

The extent to which cutaneous tests with these three antigens agree is suggestive but not absolute evidence of the specificity of the Frei test principle, contradictory clinical evidence to the contrary notwithstanding.

CONCLUSIONS

With appropriate care to avoid confusing nonspecific papules with positive reactions, it may be concluded that human bubo pus antigen, mouse brain antigen and yolk sac antigen (lygranum) are probably equally satisfactory for intracutaneous testing.

ABSTRACT OF DISCUSSION

Dr. Herman Beerman, Philadelphia: An ideal test for lymphogranuloma venereum would be one which always yields positive reactions in the presence of lymphogranuloma venereum but never gives such reactions in the absence of this disease. It would also be one that indicates whether, if the reaction is positive, the disease is in an active state. The Frei test performed with any of the present antigens falls short of this ideal, and the reliability of this procedure is still in doubt. In addition to cases in which there is clinical evidence of lymphogranuloma venereum but in which the reaction to a Frei test is negative, there are certain cases in which lymphogranuloma venereum is suspected and in which other cutaneous tests, such as the chancroidal, performed simultaneously with the Frei test may likewise give positive reactions. This has been observed not only by the opponents of the validity of the Frei test but also by those who are especially favorable to this intradermal procedure. The explanations advanced to account for these simultaneously positive results of Frei and chancroidal tests have not been entirely satisfactory. It is possible that the same phenomenon which accounts for them may be a factor underlying the close parallelism between the tests made on the same person with different types of Frei antigen, such as human and virus antigen. This may add another factor to be controlled in evaluating the comparative results of the use of various Frei antigens either from the same source or from different sources (human pus, mouse brain or chick embryo).

The Drs. Robinson have still further enhanced the usefulness of the human antigen by their attempts to standardize various batches of this substance. Their technical suggestions in regard to handling the human Frei antigen have made it possible for me to keep samples, which they have sent me, uncontaminated for a long time.

Limited experience with the mouse brain antigen has been rather disconcerting because of the lack of clearcut differences between the results with the mouse brain control and the mouse brain antigen. In this respect I agree with Binkley and his associates and Strauss and Howard but disagree with Grace and many others.

With regard to lygranum (Squibb), I have had no personal experience with it, but my associate, Dr. S. J. Axelrod, from the service of Dr. Norman R. Ingraham Jr., Philadelphia General Hospital, supplied the data in the following table:

Results of Tests for Lymphogranuloma Venereum with Lygranum

Patients	Number	Reactions		
		Positive	Doubtful	Negative
With inguinal buboes	29	14	3	12
With rectal strictures	23	15	3	5
With granuloma inguinale	4	0	1	3
Ward patients (chosen at random)	49	1	2	46
Infants of mothers with positive Frei reactions	4	0	0	4
Syphilitic pregnant women under antisyphilitic treatment	15	3	1	11
Totals	124	33	10	81

Forty-six tests were run parallel with tests with human bubo pus antigen. In forty tests the results were in complete agreement; in three tests they were in partial agreement, and in three tests there was complete discord.

The chick embryo antigen has about the same degree of specificity as the human bubo pus antigen and therefore can be considered a convenient substitute for human bubo pus antigen. In this series no symptoms of sensitivity to egg albumin were observed, and only one reaction could be definitely considered as being possibly a false positive. When reading the reaction from lygranum, Dr. Axelrod used a rigid standard: Only induration was measured. A positive reaction consisted of a papule measuring 7 by 7 mm. or larger (about one third of the positive reactions were pustular or ulcerated); a doubtful reaction was one measuring 5 to 7 mm. in diameter, and a negative reaction was a papule less than 5 mm. in diameter.

The Frei test as such is still a useful means of diagnosing lymphogranuloma venereum, although one still cannot always state whether the presenting complaint is lymphogranuloma venereum or whether the patient who has a positive reaction had the disease some time in the past.

Dr. Robert Brandt, Cincinnati: At the University of Georgia School of Medicine, Augusta, Ga., I had the privilege of working with Drs. Greenblatt, Torpin and Sanderson for about two years. We cannot agree completely with Dr. Robinson's conclusions, although the fundamental facts are identical (*Ven. Dis. Inform.*, to be published). In the average population, especially in the South, one finds a number of patients who give a strongly positive reaction without any evidence of lymphogranuloma venereum. Sometimes there are some pertaining facts in the history and sometimes not, but the latter point does not preclude previous infection. I collected cases of lymphogranuloma in which complete healing had occurred without any treatment and sometimes without any discernible scars. I think even a negative history or an absence of residues is not a priori objection to the specific character of a positive reaction. In cases in which there are clearcut positive reactions we tried to determine the possibility of nonspecificity and injected human pus from another source as a control. We never obtained a reaction of the same strength as with the specific antigen, though a slight reaction may occur.

Now, we have frequently observed simultaneous reactions to both lymphogranuloma and chancroid antigens. We thought of the mechanism of co-reaction,

i. e., high sensitivity to tuberculin may be accompanied by increased sensitivity to other substances. Our investigation demonstrated that only in the acute state of either lymphogranuloma venereum or chancroid there might be produced a co-reaction to the antigen of the other disease, but such a reaction was never present in the later phases of the diseases.

Mouse brain and egg yolk antigen are slightly less specific if used in a concentration that produces strongly positive results in the patients with lymphogranuloma venereum. But here one can avail one's self of a control antigen of exactly the same composition as the test antigen, which is not possible, of course, with pus antigen. It may be concluded that, with due consideration of clinical facts, the possible slight reactions in normal persons do not diminish the specific value of the various Frei antigens.

Dr. Maurice J. Strauss, New Haven, Conn.: Unless I misunderstood, the Drs. Robinson have stated that the Frei test is of limited diagnostic usefulness. The Frei test is in many ways comparable to the tuberculin test, and nobody feels that the tuberculin test is of limited diagnostic usefulness. Investigators who have studied lymphogranuloma venereum do not feel that the Frei test is the whole answer; they rely somewhat on the clinical picture, and an estimation of the serum proteins can be helpful. Total proteins are increased, with the greatest increase in the globulin, so that the albumin-globulin ratio is frequently reversed. The authors said that one objection to human antigen is the variation in the antigenic content of various antigens. The person who is doing the test must know something about his antigen and his patients. The Drs. Robinson do. Later in the paper they state that they use various dilutions simply because they know the antigens and have tested them.

The objection to mouse brain antigen because of nonspecific reactions is a valid one. The authors say that nonspecific reactions caused by bubo pus can be easily distinguished but that with mouse brain antigen it is frequently difficult to distinguish nonspecific from specific reactions. Let me restate the position which I took a couple of years ago in commenting on the routine use of mouse brain antigen. I feel that any test which depends for its positivity on a difference of 1 or 2 mm. in size of the reaction is not one which should be used by the average general practitioner. In our laboratory my associates and I carry millimeter scales in our pockets and have a pair of calipers for measurements. I feel that the results of this test should be read just like those of the tuberculin test. One should be able to look at a reaction and say "That is positive" or "That is negative." Frei himself told me that he did not measure the reactions. In his original description of the test he used the word *"etwa,"* which means about or nearly. That, I think, is perfectly good evidence that he did not measure these reactions.

With lygranum I have not had very much experience. There was reaction in a small number of tests which was considered nonspecific, but I have not seen reactions such as Drs. Robinson describe. I assume that the authors have checked the cases in which there were divergent results with human bubo pus and the various other antigens. I should be interested to know the serum protein levels in these cases.

I cannot completely agree with the conclusions as presented. I do not believe that mouse brain antigen is as good as human antigen for the reasons I have stated. I do not know about lygranum yet. Further studies such as these authors have presented, that is, studies on large groups of cases, are needed so that a proper conclusion about the value of various forms of antigens for the performance of Frei tests may eventually be arrived at.

Dr. Arthur W. Grace, New York: Mouse brain antigen served a useful purpose at a time when there was no adequate supply of material for the diagnosis of lymphogranuloma venereum. The newest antigen,[4] prepared by the growth of the virus in the yolk sac of the developing chick, is an almost water-clear, practically pure suspension of the granules of the virus. It is therefore the ideal material for the performance of the Frei test. In the hands of my collaborators and myself it has proved superior to mouse brain antigen both in specificity and in sensitivity. I am now convinced that mouse brain and human pus antigens are outmoded and should pass from the stage altogether.

The most delicate test for lymphogranuloma venereum is the complement fixation test recently developed by Rake. The antigen employed in the test is the same suspension of virus granules as used in the cutaneous test with yolk sac antigen. A high degree of parallelism has been found to exist between the results of the cutaneous test with yolk sac antigen and the results of the complement fixation test. After using both of these tests, my associates and I have come to the conclusion, not that yolk sac antigen yields false positive reactions, but that lymphogranuloma venereum exists in an asymptomatic as well as in a symptomatic form, of which the former is considerably the commoner.

Dr. Harry M. Robinson, Baltimore: Dr. Beerman mentioned a fact which Dr. Grace later commented on, that a better test is needed in the diagnosis of this disease. I do not believe that the Frei test has failed, because if used properly it is of value. I am not convinced that the alteration of the albumin-globulin ratio is specific, because it has been found to be present in several conditions. I believe, however, that a procedure which has not yet been mentioned today is of greater value than even the complement fixation test—that is, inverse testing. During the active phase, and that is presumably the time when the complement fixation test is of greatest value, one may excise the bubo even if it is not fluctuant or take the pus if it is fluctuant and by making an antigen of the product test it on known reactors. If the reaction to this substance is positive in 5 known reactors, one may conclude that the patient has lymphogranuloma venereum. I believe that these inverse tests, if considered in conjunction with determination of the albumin-globulin ratio, the complement fixation test and the Frei test would probably help more than any one of the methods alone.

Dr. Brandt stated that he and his associates agree with my facts and not with my conclusions. As long as they agree that they get positive reactions in a large number of cases in which there is no clinical evidence of lymphogranuloma venereum, that is the important fact. It is known that in patients with carcinoma of the rectum who have a stricture, the reaction to a Frei test is positive. In cases in which the reaction to a Frei test was positive, we found by inverse testing that in some the buboes were chancroidal. I believe that the Frei test by itself is valueless unless checked by inverse testing. It is possible that the test mentioned by Dr. Grace will supersede all of these.

Dr. Strauss mentioned the tuberculin test. I am sure he knows that the tuberculin test is not nearly as helpful in the diagnosis of tuberculous disease as many think it is and that certainly that test can be used and read only by physicians who are experts in its use. There are many cases of conditions which are tuberculous in which the reaction to a tuberculin test is negative. There are many others in which it is positive, and of course there are many in which the reactions are positive but in which there is no evidence of tuberculosis.

As far as we know, by autopsies and other investigations, many patients have had positive reactions to Frei tests who have no evidence whatever of the active disease.

ESTROGEN THERAPY OF TINEA CAPITIS

PRELIMINARY REPORT

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AND
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The rationale of the therapy of tinea capitis with estrogens is based on an observation of the tendency toward spontaneous cure at puberty and the rarity of the disease in adults. Physiologic evidence of estrogen production before puberty is insignificant, and the development of the adult type of cell in the vagina in children has been repeatedly demonstrated as the result of estrogenic therapy. These considerations prompted the organization of a clinic for ringworm of the scalp in July 1940 at the Robert B. Green Memorial Hospital to determine the effect of estrogen therapy on tinea capitis.

The multiplicity of drugs and procedures used heretofore in the treatment of tinea capitis has precluded, in general, the use of any single routine therapeutic procedure. Epilation has perhaps been the most uniform method of treatment, and even this has subjected children to hazardous methods, such as the use of thallium acetate or the application of roentgen rays by inexperienced operators. The element of time involved in the regrowth of hair has at times been distressing to the parents as well as to the physician. The answer to this problem should therefore be a method of treatment that would cause systemic changes simulating those taking place at puberty, as the phenomenon of spontaneous cure at that time has been observed for many years. On this basis the effect of estrogens was studied.

DIAGNOSTIC CRITERIA

Treatment was confined to patients who presented the classic appearance of tinea capitis. In the majority the condition was of the microsporon type. The clinical diagnosis was substantiated by microscopic examination of scales and hair. Cultures were made in doubtful cases. The following organisms were identified; Microsporon audouini, Microsporon lanosum, Trichophyton gypseum and Trichophyton violaceum.

Studies and contributions from the Robert B. Green Memorial Hospital, departments of Dermatology and Pediatrics.

Read before the Section on Dermatology and Syphilology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

METHOD OF TREATMENT

All patients seen at the clinic since July 1940 have been given estrogens. Estrone (theelin) [1] and diethylstilbestrol [2] were employed both orally and locally. Patients began treatment with no discrimination as to the choice of drugs. Conventional methods of treatment were omitted, including the use of soap and water on the scalp. Probably because of this, pyoderma of the scalp developed in 2 patients in addition to tinea capitis. One of these patients received wet boric acid packs for one week, and another received in addition a 2 per cent solution of gentian violet locally for five days.

ESTRONE

Estrone was administered orally in gelatin capsules, each containing 5,000 international units. One capsule was given daily. Local treatment consisted of the daily application of 1 Gm. of ointment containing 5,000 international units of estrone. A week's supply of the substance was given to each patient, and an attempt was made to have the patients return to the clinic at weekly intervals. The majority received combined oral and local medication. A small group, however, were given oral medication only, and a 4 month old baby was given local treatment alone. The total dose varied from 14 to 56 capsules and from 7 to 56 Gm. of ointment.

DIETHYLSTILBESTROL

Patients receiving diethylstilbestrol orally were given 3 tablets daily, each containing 1 mg. This dose represents 75,000 international units a day or 525,000 international units a week. An ointment containing 125,000 international units per ounce (31 Gm.) was used in the majority of cases in combination with oral medication. One patient received local treatment only, and 2 received tablets of diethylstilbestrol without the ointment. The total dose varied from 21 to 189 tablets and from 1 to 7 ounces (31 to 220 Gm.) of ointment.

ANALYSIS OF CASES

Thirty consecutive cases are included in this report. The patients were accepted for treatment without any attempt at selection from the standpoint of clinical types of ringworm or the type of fungus involved. Six additional patients are now under treatment, and all new ones will be given estrogen therapy as this study progresses.

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1. Parke, Davis & Co. supplied the estrone capsules and ointment.

2. Winthrop Chemical Co., Inc., supplied the diethylstilbestrol tablets and ampules.

Eighteen boys and 12 girls were treated. Of this group, 5 girls and 10 boys received estrone, while 7 girls and 8 boys received diethylstilbestrol. The ages varied from 4 months to 11 years (table 1).

San Antonio, Texas, has a large Latin American population, and for this reason 19 Mexicans, 10 white children and 1 Negro child comprised the 30 patients.

The duration of the infection varied from ten days to thirty-two weeks before estrogen therapy was given. The average was nine and four-tenths weeks for the group treated with estrone and six and three-tenths weeks for those receiving diethylstilbestrol. No relation between the rapidity of cure and the previous duration of the infection was noted in either group.

Three patients in the group treated by estrone and 1 in the group in which diethylstilbestrol was used had received previous treatment,

TABLE 1.—*Ages of Children (Eighteen Boys and Twelve Girls) Receiving Estrogen Therapy for Tinea Capitis*

Estrogen	Age of Patient											
	4 Mo.	2 Yr.	3 Yr.	4 Yr.	5 Yr.	6 Yr.	7 Yr.	8 Yr.	9 Yr.	10 Yr.	11 Yr.	
Estrone.....	1	..	..	2	4	1	2	1	4	..	..	15
Diethylstilbestrol...	..	1	1	1	3	3	1	2	1	..	2	15
Total.....	1	1	1	3	7	4	3	3	5	..	2	30

consisting of local applications of ointments obtained from druggists or physicians. Roentgen rays had not been used in any case.

EXPERIMENTAL WORK

The dose of estrone employed was necessarily empiric since there were no published reports to serve as a guide. The dose of diethylstilbestrol was suggested by a representative of the Winthrop Chemical Co., Inc. A determination of the fungicidal property of each estrogen is now in progress. Biopsies of the scalp before, during and after treatment are being made to establish the effect of the estrogens on the skin and its appendages. It has not been possible to study a large enough group so that any conclusions may be made at this time.

RESULTS

A critical analysis of the results of treatment is both difficult and hazardous because of the small number of patients treated. It is significant, however, that only 4 patients failed to obtain a clinical cure, and these were ones who discontinued treatment. Two of these were seen only once, and 1 received treatment for only two weeks. The fourth

patient was treated for four weeks, and although the child had a regrowth of hair the scalp was scaly. This patient failed to return for microscopic examination of the scales and is therefore not classified as cured. Patients who did not return for final inspection after beginning regrowth of hair had been observed in the clinic were visited in their home.

A rapid regression of the tumefaction in 2 cases of kerion of the scalp was noted. There was a considerable delay, however, in the regrowth of hair. One of these patients received estrone and the other diethylstilbestrol. The scalp remained glossy, and regrowth began in sixty-three days for 1 and fifty-two days for the other. In all the other cases scaling disappeared on an average of four to five weeks. Regrowth of hair began on an average of thirty-eight days for patients treated with estrone and thirty-eight and five-tenths days for those treated with diethylstilbestrol.

It is not possible to correlate the time of healing either with the amount of estrogen administered or with the method of its administration. One patient who was given one week's supply of the substance and no other treatment had a regrowth in fifty-five days; another was given two weeks' supply and had a regrowth in thirty-eight days, while still another was treated continually for thirty-eight days, at the end of which time a regrowth of hair was noted.

TABLE 2.—*Results of Treatment of Patients with Tinea Capitis with Estrogens: the Time at Which the First Regrowth of Hair was Observed*

Estrogen	Weeks of Treatment				
	4 to 5	5 to 6	6 to 7	7 to 8	8 to 9
Estrone	5	5	1	2	0
Diethylstilbestrol	7	3	1	1	1

Table 2 illustrates the results of treatment with estrone and diethylstilbestrol with reference to the time at which a regrowth of hair was noted. No recurrences were observed in patients from two to six months after discharge.

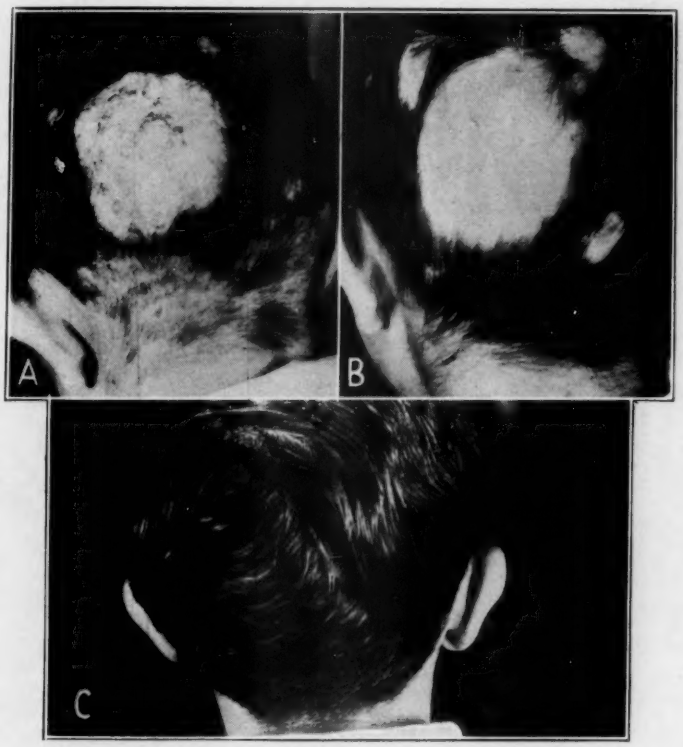
REACTIONS

No reactions were noted in the group of patients receiving local treatment with estrogens. All medication was well tolerated. Two boys receiving estrone both orally and locally had slightly tender enlargement of the breasts, which disappeared promptly after administration of this preparation was discontinued. Two girls had a similar reaction from diethylstilbestrol. In 1 of these an acute edema of the vulva developed coincident with the mastitis. This subsided as soon as administration

of the substance was discontinued. On the whole both estrogens were well tolerated, and at the time of writing no sequelae have been observed.

SUMMARY AND CONCLUSIONS

A preliminary report is made of the effect of treatment with estrogens in 30 consecutive cases of tinea capitis. No significant difference in the effect of estrone (theelin) and diethylstilbestrol was noted, the time of healing and tolerance to the drug being practically the same for both



Patient with tinea capitis, showing involvement of the scalp (*A*) before treatment and (*B*) after two weeks of estrogen therapy. *C*, complete regrowth of hair after estrogen therapy.

preparations. The mechanism of the action of the estrogens is at present unknown. It is suggested that it may be due to temporary production of cells of the adult type. This might explain the tendency to spontaneous cure of tinea capitis at puberty. If estrogen therapy can be proved to cause changes in the scalp which increase its local resistance, then it is permissible to expect that the effectiveness of this therapy might be increased by the vigorous use of fungicidal agents. Further investigation

is needed before routine treatment of tinea capitis with estrogens may be advocated for general use, because this report cannot be subjected to a critical analysis. At least the treatment is simple, as it entails only oral and local medication, no epilation being required.

NOTE.—Two cases of vaginal bleeding following estrogen therapy in girls aged 3 and 5 years respectively have been observed since this paper was submitted for publication. This reaction subsided shortly after administration of the drug was discontinued.

ABSTRACT OF DISCUSSION

DR. GEORGE M. LEWIS, New York: Therapy for patients with ringworm of the scalp is still not entirely satisfactory. However, the rationale of treatment is much better understood with correlation between clinical and laboratory observations. It is of the utmost importance to know the identity of the causative fungus in order to institute the correct treament. The observations in culture also determine the prognosis. If cultural studies reveal M. lanosum the outcome is certain to be favorable. In such cases one can predict with fair certainty that a cure will take place by means of local therapy alone in approximately two months. Some patients are cured within two or three weeks and occasionally a stubborn condition is encountered for cure of which three or four months is required.

The reference of the authors to petrolatum perhaps was in regard to an experimental series (Lewis, G. M., and Hopper, M. E.: Ringworm of the Scalp: V. Mechanism of Cure of Infections Caused by Microsporon Lanosum, ARCH. DERMAT. & SYPH. **36**:1194 [Dec.] 1937), in which Dr. Hopper and I used no other treatment except petrolatum, rubbing it on the affected scalp and washing the scalp with a stiff brush. We obtained as good results with this regimen as with the use of any fungicidal application. All the patients had infections due to M. lanosum. Our conclusions were that cure took place because the infected hairs fell out. As far as we could find out, the response was due to immunologic factors. Because of the perifollicular inflammation, epilation of the diseased hairs could be accomplished by rubbing. There is considerable evidence at hand that geographic differences are not important when such infections are present and that these conditions respond as well in Texas as in New York.

The evidence in favor of some mechanism other than an immunologic one to explain spontaneous cure and also the difference in the response to treatment of patients infected by different fungi cannot be gone into here. If there is more than the immunologic factor, the next most likely would be an endocrine factor.

In cases of ringworm of the scalp due to M. audouini, T. violaceum and Achorion schoenleinii, there is no tendency to spontaneous cure. A good result obtained in cases in which these fungi cause the condition is good evidence that the remedy used is responsible. For that reason, one of the causes cited by the authors is good evidence that their treatment is of some value. The condition in this case was due to T. violaceum. I think any one who has had the experience of trying to cure this condition knows how difficult it is to obtain a favorable result.

The authors have said that this report is a preliminary one and that in their further work they are going to control the results by using other therapeutic methods and by making cultural and immunologic studies. That will help to give a true picture of the value of their treatment. I should also like to suggest that filtered

ultraviolet rays be used to assist in determining when cure has taken place. I feel that use of such rays is indispensible in this particular and hesitate to rely entirely on clinical observations. The rays are also useful in gathering infected material and in determining the extent of the infection, particularly from the standpoint of showing the parents all the infected areas.

Dr. N. E. Aronstam, Detroit: Drs. Poth and Kaliski have amply demonstrated the efficacy of estrogens in the treatment of tinea capitis in children. For about 8 patients of my own, mostly children, I have used an estrone ointment on the lesions without other local fungicidal medication or radiotherapy, with excellent results. In all their cases a thorough microscopic search was made to determine fungi or mycelia, with positive results in all. The rationale of the modus operandi of these estrogens as propounded by the authors is both novel and ingenious and may explain the preponderance of tinea capitis in children of prepubertal age. At any rate, empirically this form of treatment is valuable and should be used before local medication or radiotherapy is resorted to.

Dr. Theodore Cornbleet, Chicago: The normal skin does not contain vitamin A. Nonetheless this vitamin is important for the proper functioning of the skin. Deficiencies or abnormal usage produce characteristic cutaneous disorders and dysfunctions. Investigators, including myself, have not found any of the estrogens on the surface of the skin. The skin can, however, absorb these materials when they are applied on the surface. Doubtless estrogens in the body affect the physiologic condition of the skin in a way similar to that in which systemic metabolism of vitamin A affects the skin. This does not mean that any effect seen after local application of estrogens takes place locally. Nor does it even mean that such local therapy is the most rational variety. What is known seems to indicate that if estrogenic therapy eradicates ringworm of the scalp, the manner of its action is systemic. For that reason the estrogen ought probably to be administered by mouth or parenterally and not locally, so that definite doses can be more accurately given. Besides, publicizing such local therapy incites self medication with patent remedies, with its attendant dangers. I am prepared to believe, because of spontaneous cure of tinea of the scalp at puberty, that a child is susceptible to this infection because he has less estrogen than does the adult. If this work of Drs. Poth and Kaliski is substantiated, it represents another triumph over another common and stubborn disease with modern weapons.

Dr. C. Ferd. Lehmann, San Antonio, Texas: I have had the opportunity to see a few, if not all, of this series of patients. I am struck by a few points in the follow-up study of these, particularly concerning the regrowth of hair. What seems perfectly marvelous to me is the acceleration of the regrowth of hair and the lack of toxicity of these substances in doses which would produce marked symptoms in adults.

Drs. Poth and Kaliski are to be commended for bringing this subject to attention, particularly the principle to make an effort in changing the soil, the host, on which the organism grows. From what I have seen of this work, I think that the results are very encouraging. The authors have picked a group of patients that furnish a fine series of controls, that is, a group that is living under poor hygienic conditions, who, if one ever can get them with any other treatment, commonly have recurrences. In spite of the poor hygienic conditions under which these patients are living, Drs. Poth and Kaliski have a means of getting them symptomatically or clinically well faster than any other means ever used at the Robert B. Green Memorial Hospital. I want to stress again—

this has been stressed before, and I have pointed this out before—that the types of ringworm encountered at this clinic are much more recalcitrant than any others to the accepted and tried local means of treatment.

Dr. Duncan O. Poth, San Antonio, Texas: We appreciate the remarks of Dr. Lewis. We are to cooperate with him in the work for the coming year. Dr. Aronstam reported cures with the use of estrone locally. We have several patients who were cured this way; however, the majority received estrogens orally.

Recently there appeared a report (Chamberlin, T. L.; Gardner, W. U., and Allen, E.: Local Responses of the "Sexual Skin" and Mammary Glands of Monkeys to Cutaneous Applications of Estrogen, *Endocrinology* **28**:753 [May] 1941) on the local application of estrone to one breast of a male monkey. An alcoholic solution was used and one application made daily. Within four days hyperemia of the nipple of that breast was noted; within two weeks' time it had doubled in size with heavy pigmentation, and there was only slight enlargement of the opposite breast. I believe that this work will answer Dr. Cornbleet's question about local treatment. Estrogens have no effect on the appetite, growth or general status of children. Dr. Lehman's remarks coincide with our observations.

This has been a most interesting study, and we feel that there are many possibilities and certainly a great many problems still to be solved.

DYSKERATOID DERMATOSIS

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AND
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The term dyskeratosis as used by the dermatopathologist is defined as a process in which there is an alteration in the life cycle of the epidermal cells. It may be a benign process, as seen in keratosis follicularis (Darier) and molluscum contagiosum, or a malignant one, as seen in Paget's disease or Bowen's disease.

The dermatosis herein described is one in which the microscopic picture of the entire epidermis closely resembles that of a dyskeratotic process. For true dyskeratosis to occur, by definition, there must be adequate time for cellular aging and cellular division. However, in the condition described in this paper it has been observed that a somewhat similar microscopic picture may develop within one hour.

This condition was described in March 1939 by Pels and Goodman [1] as "keratosis follicularis with vesiculation," by Hailey and Hailey [2] in April as "familial benign chronic pemphigus" and by Ayres and Anderson [3] in September as "recurrent herpetiform dermatitis repens." Hailey and Hailey were the first to recognize this as a distinct entity. In August of the same year Goodman [4] pointed out that his study of the cases described by Hailey and Hailey "lead inescapably to the conclusion that they were dealing with Darier's disease of the rare vesicular and bullous type," which he had previously described with Pels.[1] Ayres and Anderson [3] in a footnote in their publication stated that after a careful study and examination of the Hailey and Hailey report they "are of the opinion that the disease entity which Drs. Hailey describe is of exactly the same nature" as the ones they described. We are also of the opinion that

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From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

Read before the Section on Dermatology and Syphilology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

1. Pels, I. R., and Goodman, M. H.: Criteria for the Histologic Diagnosis of Keratosis Follicularis (Darier): Report of a Case with Vesiculation, Arch. Dermat. & Syph. **39**:438-455 (March) 1939.

2. Hailey, Howard, and Hailey, Hugh: Familial Benign Chronic Pemphigus, Arch. Dermat. & Syph. **39**:679-685 (April) 1939.

3. Ayres, S., Jr., and Anderson, N. P.: Recurrent Herpetiform Dermatitis Repens, Arch. Dermat. & Syph. **40**:402-413 (Sept.) 1939.

4. Goodman, M. H.: Familial Benign Chronic Pemphigus, Arch. Dermat. & Syph. **40**:272 (Aug.) 1939.

these cases and those we are reporting are all instances of the same entity.

Pels and Goodman [1] stated that Bukovský [5] and several others appear to have described this many years ago as a vegetative or vesicular variant of keratosis follicularis.

Hailey and Hailey [6] in a second report described an additional 22 cases occurring in four generations of two separate family groups, 13 and 9 in each. In the discussion, Dr. Howard King objected to classifying the disease in these cases as pemphigus, and Dr. A. B. Loveman suggested that the name be altered to "chronic familial pemphigoid dermatitis." Dr. Howard Hailey indicated that this title had already been suggested by Dr. Fred Wise.

Franks and Traub [7] in April 1941 reported 2 cases and suggested that this disease be regarded as a definite entity. They objected to the term "pemphigus" and offered "familial benign chronic bullous dermatosis."

Since the recent recognition of this dermatosis, several patients have been seen at various society meetings throughout the country. Sweitzer [8] presented a case of "keratosis follicularis" at a meeting of the Minnesota Dermatological Society. He expressed the opinion that the microscopic observations in this case were identical with those described by Pels and Goodman.[1] Becker and Obermayer [9] showed a patient in whose family 27 cases in three generations were traced. They offered the designation "dyskeratosis bullosa hereditaria." Anderson,[10] Ayres and Rogers,[11] Lynch [12] and Rein [13] have presented cases. Anderson maintained the

5. Bukovský, J.: Psorospermosis follicularis vegetans Darier, Arch. f. Dermat. u. Syph. **75**:279, 1905.

6. Hailey, Howard, and Hailey, Hugh: Familial Benign Chronic Pemphigus: Report of Thirteen Cases in Four Generations of a Family and Report of Nine Additional Cases in Four Generations of a Family, South. M. J. **33**:477-481 (May) 1940.

7. Franks, A. G., and Traub, E. F.: Familial Benign Chronic Bullous Dermatosis, Arch. Dermat. & Syph. **43**:657-663 (April) 1941.

8. Sweitzer, S. E.: Keratosis Follicularis, Arch. Dermat. & Syph. **40**:1068 (Dec.) 1939.

9. Becker, S. W., and Obermayer, M. D.: Bullous Disease, Bullous Darier's Disease (Pels and Goodman): Familial Benign Pemphigus (Hailey and Hailey); Herpetiform Dermatitis Repens (Ayres and Anderson), Arch. Dermat. & Syph. **41**: 1170-1172 (June) 1940.

10. Anderson, C. R.: Senear-Usher Syndrome (Pemphigus Erythematoides: Chronic Benign Familial Pemphigus; Herpetiform Dermatitis Repens of Ayres and Anderson), Arch. Dermat. & Syph. **42**:489-490 (Sept.) 1940.

11. Ayres, S., Jr., and Rogers, J. D.: Recurrent Herpetiform Dermatitis Repens, Arch. Dermat. & Syph. **42**:491 (Sept.) 1940.

12. Lynch, F. W.: Benign Pemphigus (Hailey and Hailey), Treated with Sulfathiazole, Arch. Dermat. & Syph. **43**:736 (April) 1941.

13. Rein, C. R.: Familial Benign Pemphigus (Hailey and Hailey), Arch. Dermat. & Syph. **44**:963 (Nov.) 1941.

point of view that this condition was an example of the Senear-Usher syndrome (pemphigus erythematodes). Lynch found a pure culture of Staphylococcus pyogenes aureus in an unruptured vesicle in his patient and reported successful temporary relief with the use of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) orally and locally.

Our interest in the cases herein reported lies not so much in the fact that we are describing a possibly new entity but rather in the opportunity to correlate the conditions in the aforementioned cases under one descriptive term which characterizes the most outstanding and constant microscopic observation, i. e., a dermatosis in which there is a rapid development of changes suggestive of dyskeratosis. We have therefore selected for this dermatosis a neutral name of dyskeratoid dermatosis.

REPORT OF CASES

CASE 1.—E. R., a white man aged 50, a native of the United States, a broker, first consulted us in January 1939 regarding his eruption of more than thirty years' duration.

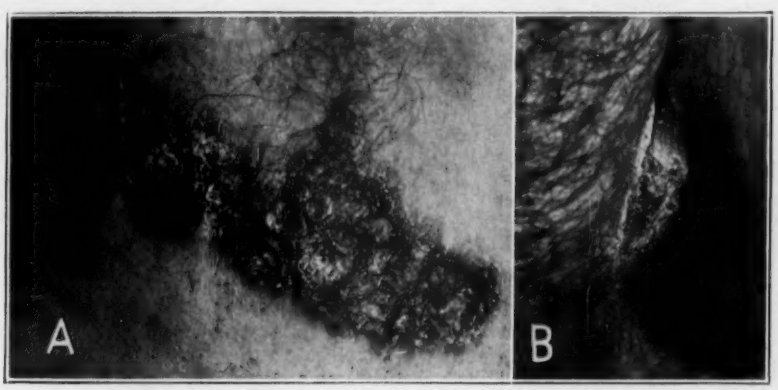

Fig. 1 (case 1).—Characteristic appearance of lesions in the right axilla (*A*) and in the left groin (*B*).

Family History.—The patient's history reveals that his father, who died at the age of 69 after his gallbladder had ruptured, had "skin trouble" of forty-five years' duration involving the collar area of the neck. The patient stated the belief that this eruption was identical with his own condition. His father was free of the eruption for as long as a year at a time and as far as he knew never sought medical attention. The patient had one brother, aged 45, and no sisters. His brother had a similar eruption, of twenty years' duration, affecting the neck area and both axillas, for which he received various forms of local and general therapy with little or no relief. He also had periods of freedom lasting for as long as a year. The rest of the patient's family history was irrelevant in reference to any eruption as far as he could remember.

Past History.—The patient stated that he had had recurrent attacks of "rheumatism" since 1915. One of these attacks resulted in ankylosis of the left wrist. About thirty years ago an acute gonorrheal urethritis developed, for which he received immediate treatment. With the exception of having had the aforemen-

tioned disease and the eruption, he was in excellent general health. His habits were temperate.

Cutaneous Condition.—The eruption first appeared thirty years previously and involved the collar area of the neck. He used various proprietary preparations with transient relief. He had periods of freedom (similar to those of his father and brother) for as long as one year. He volunteered the information that any form of local irritation produced "blisters." For the first twenty years the eruption was limited to the neck area; then a similar eruption began to appear in the axillas and groins. After that the eruption recurred on the neck and in the axillas and groins at various intervals. He received various forms of local medica-

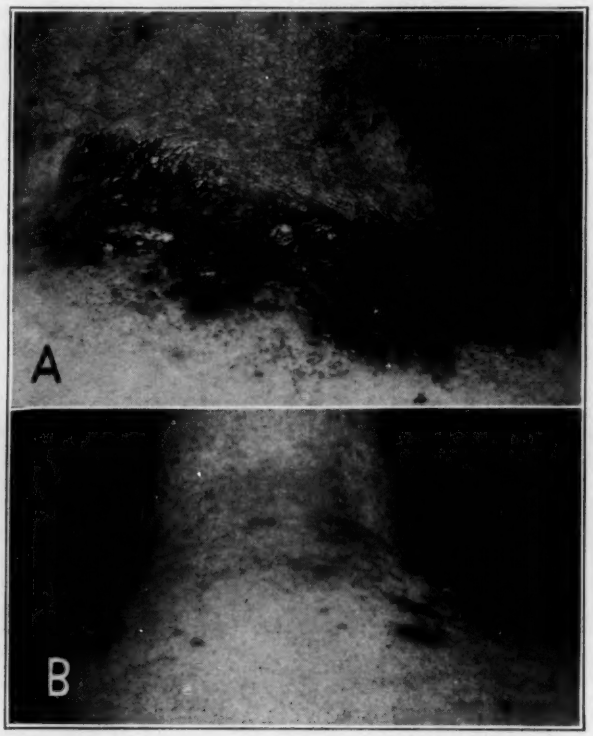

Fig. 2 (case 1).—*A*, characteristic lesions on the back of the neck. *B*, local reaction produced by gentle rubbing. The photograph was taken ten minutes after the trauma. This area appeared the same as the lesion in figure 2 *A* in a few hours. The two scars on the right were sites of removal of tissue for serial sections.

tion and injections, as well as ultraviolet and roentgen irradiation. He stated that he obtained the most rapid relief from roentgen irradiation. The results of numerous intradermal and patch tests were not significant. He was also given arsenic and salicylates by mouth with no effect. Occasionally he took phenolphthalein cathartics without altering the eruption.

Subjectively, he experienced a slight burning sensation at the site where the eruption would ultimately develop. Within a few hours there appeared a reddened area, and this was followed shortly by the development of blisters and crusts. At times these lesions were extremely pruritic, while at other times only slightly so.

The eruption consisted of discrete and confluent erythematous eczematoid patches. The individual areas were made up of isolated and coalesced vesicles and pustules, most pronounced at the periphery. Many of the vesicles had ruptured and were covered with yellowish brown impetiginous crusts. The areas showed some central involution with a pigmented residuum (figs. 1 and 2 A).

At times a Nikolsky sign was elicited on a previously involved area (neck), but it was never possible to produce this phenomenon on sites where no eruption had ever been present.

Complete physical examination, including study of the eyes, showed no abnormalities.

Treatment.—The patient received various salves, ointments, lotions and fractional doses of roentgen rays as well as oral medication, including solution of potassium arsenite U. S. P., calcium gluconate and vitamin therapy. In addition, he was given intravenous injections of calcium. It was observed that two or three fractional doses of roentgen rays produced a rapid involution of the lesions. These treatments did not prevent the subsequent recurrence of lesions. He seemed to respond most favorably to massive doses of vitamins A and D (120,000 and 10,000 U. S. P. units respectively) daily. However, the patient stated that he had had similar periods of remission under various forms of therapy and also under no therapy at all.

Laboratory Observations.—A urinalysis on Jan. 16, 1939 showed no abnormalities. Examination of the blood on February 6 revealed the following values: red cells, 4,650,000; hemoglobin (Sahli method), 100 per cent; white cells, 6,600; polymorphonuclear leukocytes, 50 per cent; lymphocytes, 41 per cent; eosinophils, 1 per cent; monocytes, 6 per cent; basophils, 2 per cent; blood sugar, 93 mg. per hundred cubic centimeters, and results of Wassermann, Kline and Mazzini tests for syphilis, negative.

Pels-Macht tests, as performed by the originators of the test, gave indexes of 44 per cent on Jan. 10, 1940 and 43 per cent on April 5.

The patient's blood was type IV (Moss).

Examination of the lesions for fungi on various occasions with cultures and slide technic and trichophytin tests gave negative results.

The following case has additional interest in view of the sequence of events that led to its discovery. A random microscopic slide was selected by one of the students in the dermatopathology class in the New York Post-Graduate Medical School and Hospital and shown to the instructor, Dr. Wilbert Sachs. At the time Dr. Sachs was in the midst of a study of the material obtained from case 1 and readily recognized the picture as representing this entity, although another diagnosis had originally been made. The patient was traced and found, and subsequent observations verified Dr. Sachs's original contention.

CASE 2.—J. T., a white man aged 25, born in the United States, a truck driver, complained of a dermatosis of six years' duration.

Family History.—The patient's father, mother, two brothers and two sisters were living and well, and none of them had a similar disease of the skin. However, a maternal cousin, the same age as the patient, had a similar eruption, which also started six years previously and which involved the same areas as did that of the patient.

Past History.—The history was essentially irrelevant. There was no history of allergy in the patient or in his family. He stated that he had had no venereal or other infection and no symptoms of any.

Cutaneous Conditions.—The eruption first appeared on the patient's neck, and four years ago it appeared in the groins and axillas. There were periods of remission at various sites, but at no time was he entirely free of this condition. The patient volunteered the information that any "rubbing" of his skin would cause him to "break out." Consequently, he habitually wore soft collars, kept open at the neck. He had been seen by several physicians and stated that he received the most relief from roentgen irradiation. However, lesions recurred in spite of this therapy. Subjectively, the patient complained of moderate itching and burning at the onset of the appearance of a lesion.

The eruption involved the neck, axillas and groins. The lesions were roughly circular, and some of them had serpiginous outlines. There was a dusky erythema present in the center of the lesions, and the edges were slightly elevated and crusted with a yellowish brown exudate. The Nikolsky sign was readily elicited on sites previously involved but could not be produced on areas where no previous eruption had been present.

Treatment.—The patient received massive doses of vitamins A and D, similar to those received by the first patient (case 1), with no relief.

Laboratory Observations.—Examination of the blood on March 18, 1940 revealed the following results: Red cells, 5,410,000; hemoglobin, 104 per cent; white cells, 7,800; polymorphonuclear leukocytes, 68 per cent; lymphocytes, 32 per cent; monocytes and basophilic or eosinophilic polymorphonuclear leukocytes, none, and reactions to serologic tests for syphilis, including the Wassermann, Kline and Mazzini tests, negative.

Blood for a Pels-Macht test taken on March 17, 1940 gave a reading of 53 per cent.

CASE 3.—Miss E. H., a white woman aged 34, first consulted Dr. Julius Raab on Jan. 3, 1940, because of a dermatosis involving the neck and the axillas of eight years' duration. At the onset the patient had periods of complete freedom from the eruption for many months, but during the last few years these intervals were shortened to about three months. For the first four years only the sides of the neck were involved, but during the past three years the axillas have also become affected.

Familial History.—Her father died at the age of 39, after the rupture of a gastric ulcer. Her mother was 58 years of age and in good health except for a chronic dermatitis of her palms. She had one brother, aged 29, who had never had any trouble with his skin. Further investigation into the patient's family did not reveal anything of significance.

Past History.—Her past history was essentially insignificant. The menses began at the age of 13, were always regular and were of the twenty-eight day type of four days' duration. The patient stated that during the first few years the eruption always cleared up spontaneously within a few days after the cessation of her menstrual period. Stumps of tonsillar tissues were removed several years ago. She never had any previous disease of the skin. The personal and familial allergic history was irrelevant. The patient has received intermittent medical care since the onset of the eruption. She has applied various lotions, salves and ointments and has received injections and ultraviolet and roentgen irradiation. There is always a remarkable improvement of the eruption following two or three exposures to roentgen rays of fractional dosage.

Laboratory Examinations.—Chemical examination of the blood and serologic examinations for syphilis gave negative results. The urine and basal metabolic rate were normal.

Physical Examination.—The general physical examination gave essentially negative results. The patient had a dermatosis localized on both sides of the neck and in both axillas. On the neck the eruption consisted of discrete and confluent erythematous plaques, measuring 3 to 4 cm. in diameter. At the periphery of these plaques were discrete vesicles, some of which had ruptured, leaving eroded areas, and some were covered with an adherent brown crust. The eruption was superficial and left no scars but showed a pigmented residuum on healing. There was a similar but less extensive dermatosis involving the axillary folds. In the pits of the axillas there were numerous discrete and confluent soft, noninfiltrated, spongy, brown-pigmented keratoses. The patient also presented numerous lentil-sized soft brown papillomas on the sides of the neck. She first noticed them a few years ago.

EXPERIMENTS

Subsequent observation of these patients revealed that the elementary lesion is an erythematous macule which soon becomes vesicular. The lesions appear only at certain sites which are especially predisposed to friction. The following experiments were performed on several occasions in case 1.

The patient was instructed to stroke 1 square inch of skin on the left side of his neck (a site of predilection) and on the right leg (an area in which no eruption had ever appeared) for two minutes at bedtime. Both of these areas appeared clinically normal at the onset of this experiment. Before the alloted time the patient had to stop rubbing the neck because the skin had become irritated and sore. He was seen eleven hours later, at which time he already presented a heavily crusted eczematized area at the site of the induced trauma on the neck. The area on the leg, however, showed no change despite the fact that he was able to rub it more vigorously for the full two minutes.

The second experiment was performed in our presence. An apparently normal area on the back of the neck was gently stroked two hundred times with the index finger for ninety seconds by one of us. During the first few seconds of this rubbing there developed an area of erythema (fig. 2*B*) which persisted and ultimately went on to vesiculation and crusting. An area on the right leg was similarly stroked three hundred times for one hundred and thirty-five seconds without any apparent change being produced in the skin. This indicates that the amount of trauma required to produce the eruption in the predisposed areas is exceedingly slight.

Tissue was excised for microscopic examination from a lesion of two days' duration on the right side of the neck in case 1. Another biopsy specimen was taken from the lesion produced mechanically by gentle stroking eleven hours previously.

Later a series of biopsy specimens were taken. Three areas were selected: Area A, on the back of the neck (a previously involved area which appeared clinically normal at the time of this experiment); area B, in the right axilla (also a previously involved area; it appeared quiescent but presented some evidence of roentgen ray sequelae, namely, pigmentation and telangiectasia), and area C, on the posterior aspect of the right leg (an area in which this dermatosis had never appeared). The latter area was used as the control in this study. The wounds resulting from removal of tissue in areas A and C were not sutured in order to permit additional removal of specimens from the edges for serial examination. The open wounds were covered with sterile dry dressings. The wound in area

B was sutured because the purpose there was merely to ascertain what effect excess roentgen irradiation had on this area. One hour after the tissue was removed for biopsy from area A additional tissue was taken from the edge of the open wound, which was designated "A, 1 hour" Additional skin (A, 3 hours) was removed from the edge of the open wound two hours later. This procedure was repeated after five and seven hour intervals (A, 5 hours and A, 7 hours). The biopsy wound was reanesthetized before each removal of additional tissue.

Another series of biopsy specimens were taken from a site (area D) on the back of the neck, 3 cm. below area A under the following conditions: This area was gently stroked with the index finger two hundred times for ninety seconds. One hour later tissue (D, 1 hour) was removed for microscopic examination. Additional tissue was removed at three, five and seven hour intervals (D, 3 hours; D, 5 hours, and D, 7 hours).

The control series of biopsy specimens were taken from area C. The original wound in area C was stroked three hundred times for one hundred and thirty-five seconds immediately after the first specimen of tissue was removed. One, three, five and seven hours later skin was removed from the edges of the wound for microscopic examination (C, 1 hour; C, 3 hours; C, 5 hours and C, 7 hours).

A portion of tissue was removed from a lesion of more than three months' duration on the back of the neck in case 2. A routine specimen was also taken from case 3.

All of the biopsy specimens herein described were taken under local anesthesia, induced with a 2 per cent solution of procaine hydrochloride containing epinephrine.

MICROSCOPIC OBSERVATIONS

Histologic examination (low power magnification) of tissue removed from a lesion of two days' duration that had appeared spontaneously in case 1 revealed the following picture: Extending across most of the section and entirely within the epidermis there was a large bullous lesion. The floor of the cavity was formed by a single row of basal cells except in a few places where the rete pegs were still present, and here there were several layers of cells. The roof of the lesion was formed by the entire epidermis above the basal cell layer, that is, by prickle, granular and horny cells, with no changes in these parts. The bulla contained fluid and a few epithelial cells from the edges of the lesion. The vessels of the upper part of the cutis and the papillary bodies were dilated and there was a moderate focal and diffuse cellular infiltration of small round cells and polymorphonuclear leukocytes, including eosinophils. The papillary bodies were well formed and covered only by the basal cell margin, thus forming part of the base of the bullous lesion above. The capillaries of the papillary bodies were greatly dilated, and many of them were filled with blood cells (fig. 3). The elastic tissue (Weigert stain) was missing in the subepidermal region (fig. 4).

Under high power magnification the basal cell margin was of normal structure, that is, the cells were columnar in shape and took a normal stain. There was a pronounced intercellular edema. The cells were separated by somewhat exaggerated interspaces, and the outline of each cell became distinct. Above the basal cell margin the cells were round, slightly larger and distinctly separated from one another. The prickles between them were entirely lost, and many of them lay free in the cavity. The nuclei of these cells were oval or round and well stained. The nucleoli were present. The cell bodies showed some abnormalities in their staining quality; some were slightly more acidophilic and a few were more basophilic. Nowhere were there any vacuolated cells or *corps ronds*. There was a fair number of mitotic figures (fig. 5).

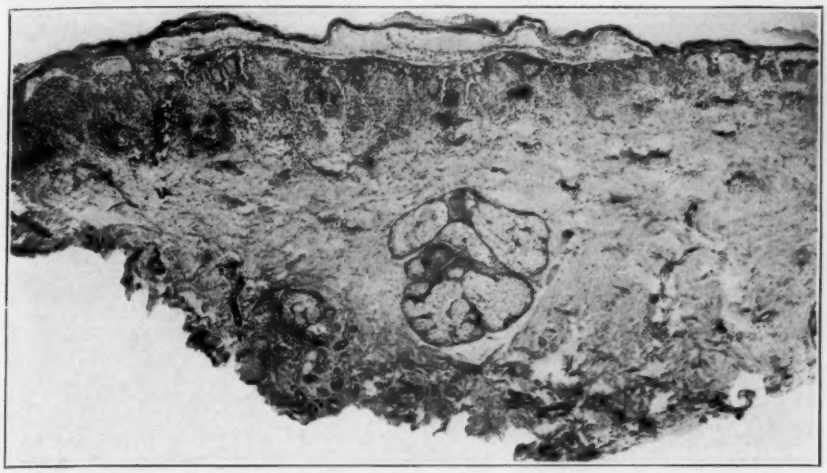

Fig. 3 (case 1).—Photomicrograph (× 30) of tissue removed from a lesion of two days' duration indicating a large vesicle in the epidermis.

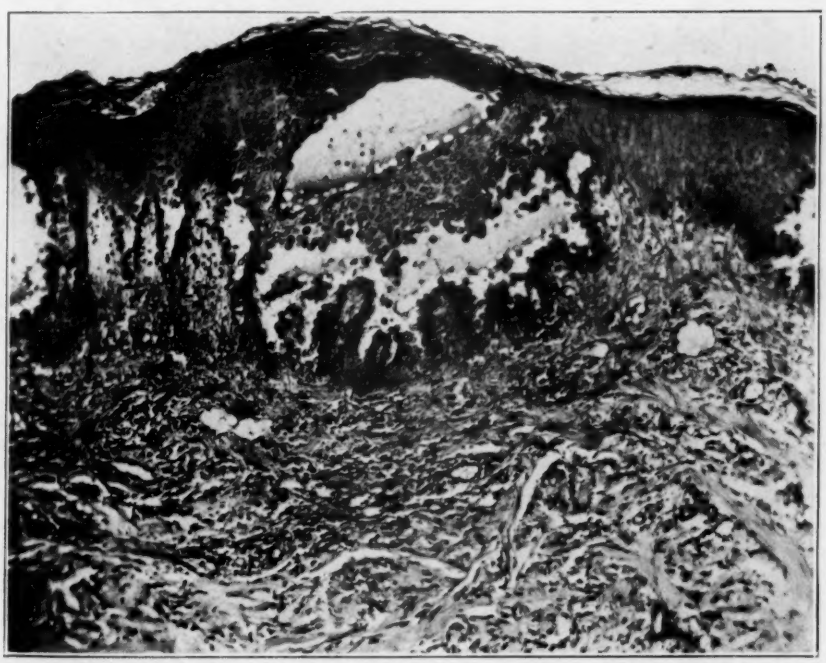

Fig. 4 (case 1).—Elastic tissue (Weigert) staining of a two day old lesion (× 80). The lack of elastic tissue in the subepidermal region is to be noted. Also the intact basal cell margin serving as the base of the vesicle is demonstrated in this section.

Examination (low power magnification) of tissue removed (case 1) from a lesion which had been induced by mechanical stroking eleven hours previously revealed that here, also, the chief pathologic process was in the epidermis. There were several small cavities within the epidermis; the base was composed of well formed papillary bodies, over which was attached a single row of basal cells, and between these the rete pegs were present. The roof either was formed by remaining epidermis or in some places was entirely missing. There was nothing special about the content of the cavity. The vessels of the middle and upper parts of the cutis were dilated, and some were filled with blood elements. There was a moderate focal and diffuse cellular infiltration composed of small round cells, many polymorphonuclear cells (numerous eosinophils) and an occasional plasma cell. There

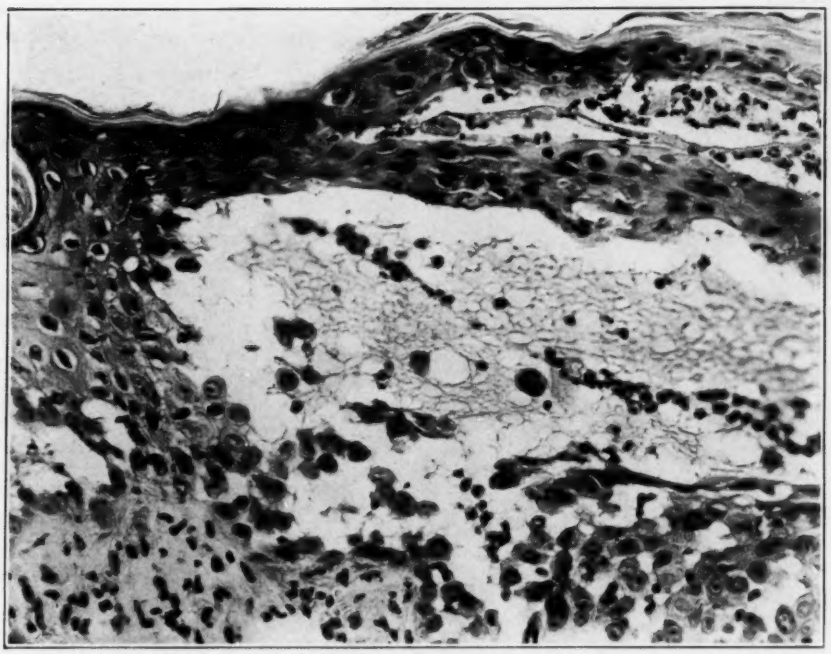

Fig. 5 (case 1).—High magnification of tissue in figure 3 (× 290), showing a large vesicle and changes in the size, shape and tinctorial quality of the cells.

was a moderate interstitial edema. The elastic tissue was wanting in the subepidermal region.

High power magnification showed that throughout most of the epidermis the cells were definitely separated by considerable intercellular edema but the prickles were present. Where the edema was greatest the cells lost their polygonal shape and tended to become round and lose their prickles. Nowhere, even in the areas of the small cavities, were there any *corps ronds*. There was no acanthosis, but there were a moderate number of mitotic figures (fig. 6).

Area A was tissue removed from the back of the neck in case 1 from an area that had been previously involved but which appeared to be clinically normal at the time of the removal. Specimens A, 1 hour, 3 hours, 5 hours and 7 hours were removed from the edges of the biopsy wound of area A at intervals of one,

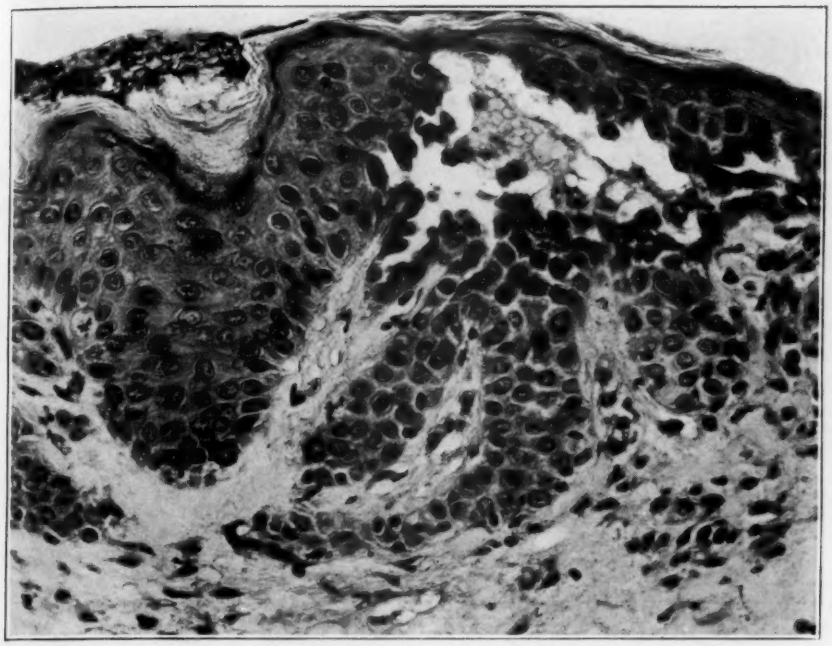

Fig. 6 (case 1).—Photomicrograph (× 325) of a lesion of eleven hours' duration. A small vesicle is shown, and changes in the size, shape and staining of the cells are demonstrated.

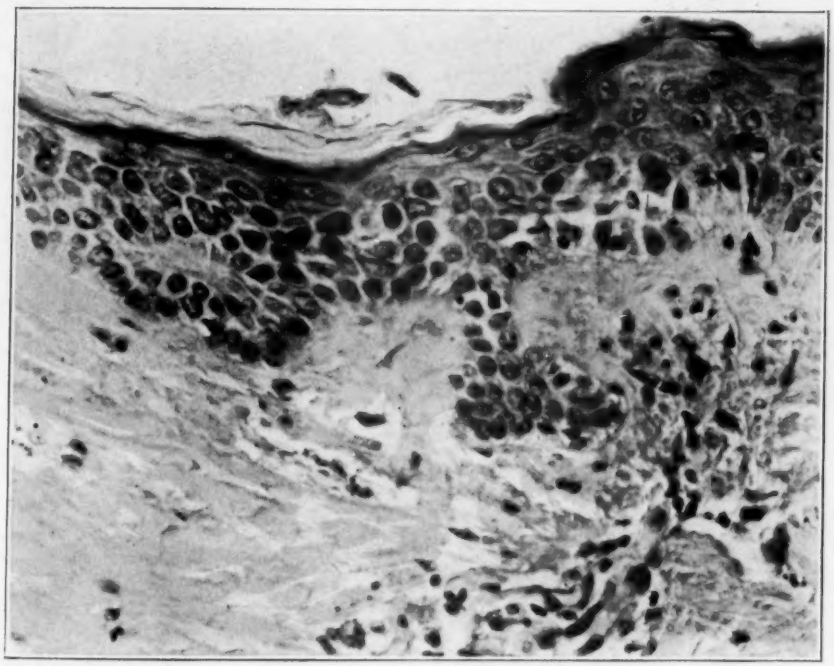

Fig. 7 (case 1).—Photomicrograph (× 85) of tissue from the back of the neck from a previously involved area that was clinically normal at the time the tissue was removed (area A). The lack of cellular cohesion and epidermal space formation is shown.

three, five and seven hours, respectively, as explained previously. The following microscopic observations were made:

Area A: There was some indication of edema of the epidermis, as evidenced by a lack of cohesion of the epidermal cells. This was manifested by small epidermal spaces. The prickles were present. There were no *corps ronds*, and the cells were not free from one another but tended toward more rounded shapes. There was no acanthosis present. There was no change in the granular layer, and no parakeratosis was present (fig. 7). The elastic tissue appeared to be missing in the subepidermal region (fig. 8). The cutis showed a mild superficial inflammatory process.

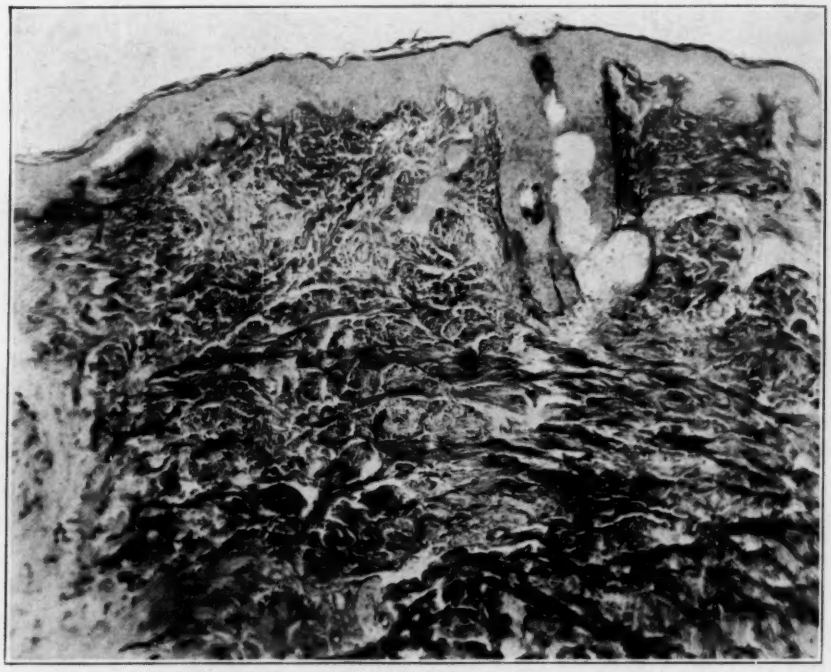

Fig. 8 (case 1).—Elastic tissue staining of tissue shown in figure 7. Note the absence of elastic tissue in the subepidermal region.

A, 1 hour: The picture was similar to that of area A, except that there was a definite vesicular lesion. Some of the cells were free in the cavity and tended to be more rounded with a loss of their prickles. There were also more congestion of the superficial vessels and slightly more pronounced cellular infiltration.

A, 3 hours: This picture was more striking than that of A, 1 hour and showed decided changes in the epidermal cells and definite vesicles.

A, 5 hours: The picture was practically the same as that of A, 3 hours.

A, 7 hours: The picture was the same as that of A, 3 hours.

Area B was a portion of tissue removed from the right axilla in case 1. This area appeared quiescent at the time of the removal of the tissue but had previously been involved with this dermatosis. This tissue was removed for study because this site showed some sequelae of roentgen irradiation, namely, pigmentation and

telangiectasia. The histologic picture was the same as that of area A except for telangiectasia.

Area C refers to an area on the right leg on which this dermatosis had never appeared spontaneously and in which it had not been possible to induce a lesion by means of trauma. Immediately after the portion of tissue was removed the area was stroked three hundred times, in one hundred and thirty-five seconds, and portions of tissue were removed at one, three, five and seven hour intervals (C, 1 hour; C, 3 hours; C, 5 hours and C, 7 hours). There were no noteworthy pathologic changes in any of the specimens except in C, 7 hours, in which slight congestion was present.

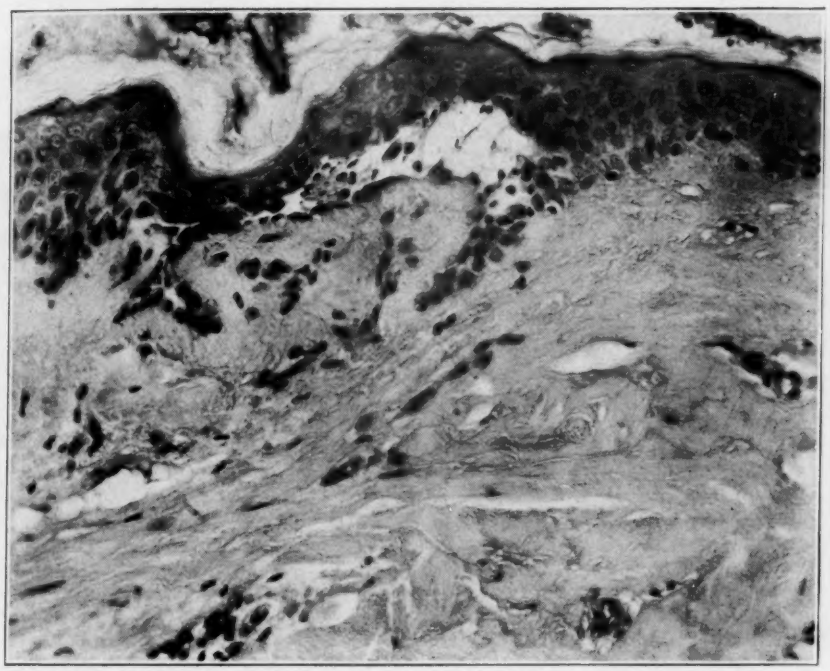

Fig. 9 (case 1; D, 1 hour).—Photomicrograph of tissue removed from the back of the neck (predisposed site) one hour after gentle rubbing. Epidermal spaces and early vesicle formation are seen. The size, shape and tinctorial quality of the epidermal cells at the vesicle margin already show dyskeratosis-like (dyskeratoid) changes.

A previously involved area 3 cm. below area A, having the same appearance as area A and appearing normal at the time of the experiment, was stroked two hundred times by gentle pressure with the index finger over a period of ninety seconds. Portions of tissue were removed at one, three, five and seven hours (D, 1 hour; D, 3 hours; D, 5 hours, and D, 7 hours), and the following microscopic observations were made:

D, 1 hour: In many areas the superficial epidermal cells were absent, in some places down to the basal cell layer. There was a lack of cellular cohesion, and several epidermal spaces were present. Early vesicle formation was seen. The epidermal cells tended to become rounded (fig. 9). There was a mild superficial

exudative inflammatory process in the cutis. The elastic tissue was missing in the subepidermal region.

D, 3 hours: There was a little more inflammatory reaction in the cutis, and a vesicle was definitely formed in the epidermis (fig. 10). The elastic tissue was missing in the subepidermal region.

D, 5 hours: Large fully formed epidermal vesicles have appeared. Cells were loose in the vesicle space and were more rounded, and prickles were lost. Some of the cells took a deeper acidophilic stain; others were more basophilic. No further changes were noted in the cutis, as compared with D, 3 hours.

D, 7 hours: The picture was the same as that of D, 5 hours.

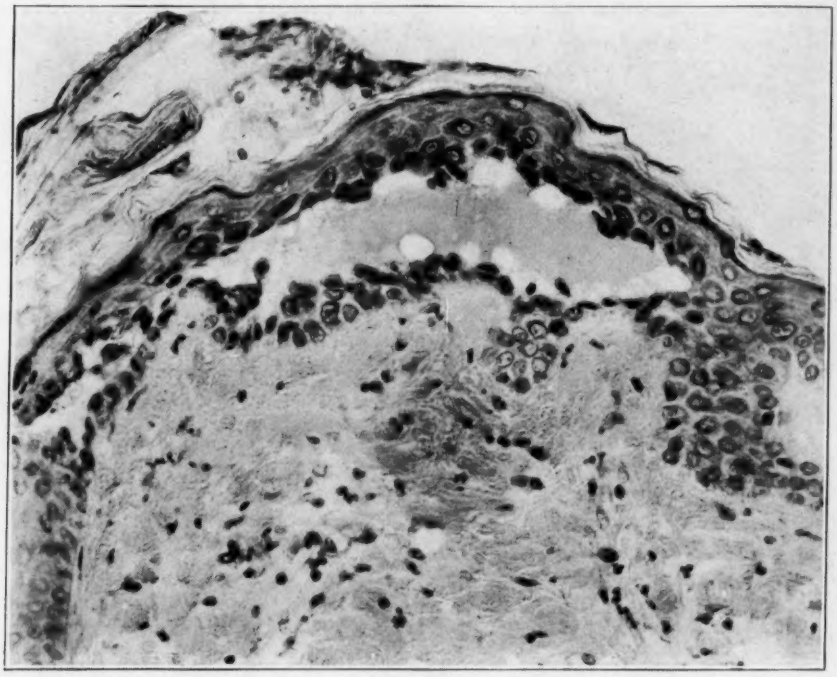

Fig. 10 (case 1; D, 3 hours).—Photomicrograph of tissue removed from the back of the neck (predisposed site) three hours after gentle rubbing. A definite vesicle is seen with changes in the size, shape and staining quality of the cells at the margin of the vesicle.

The microscopic pictures of the tissue from a lesion of three months' duration in case 2 and from a lesion in case 3 (figs. 11 and 12) were identical with those seen in fully developed lesions in case 1, previously described.

In recapitulation the outstanding pathologic observations are the following:

1. Tissue removed from areas that had previously been involved but had appeared normal clinically revealed some slight but definite changes, that is, an apparent lack of cohesion of the epidermal cells and small epidermal spaces.

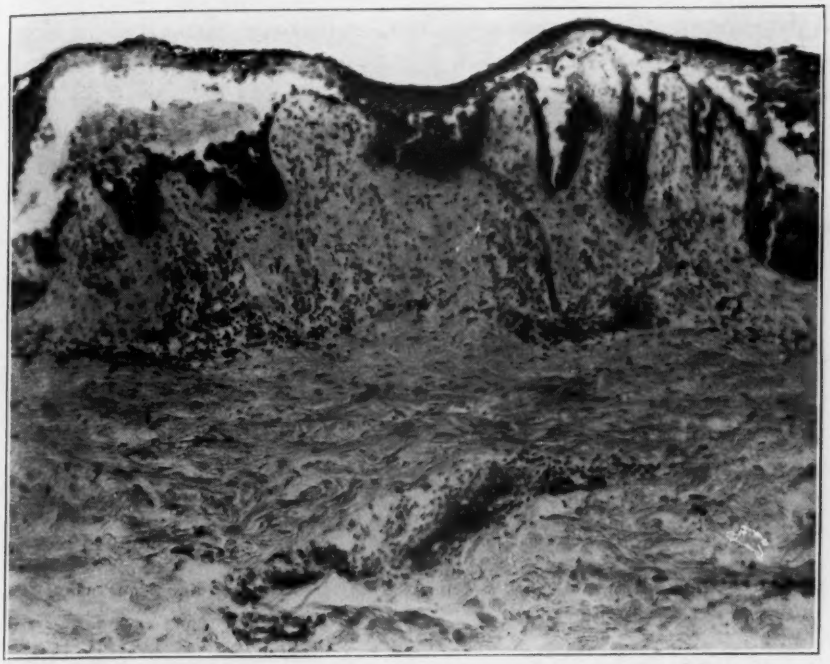

Fig. 11 (case 3).—Photomicrograph (× 95) showing typical vesicles beginning at the basal cell margin.

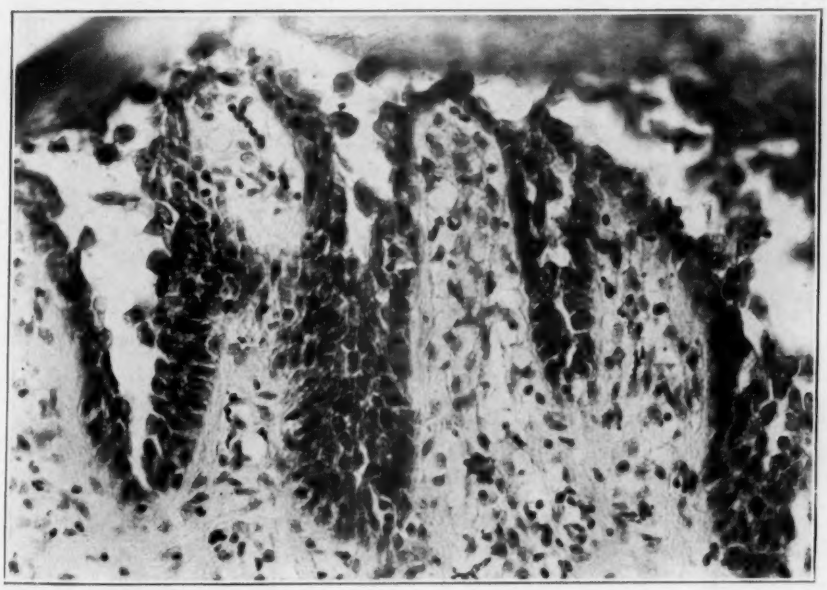

Fig. 12 (case 3).—High power magnification (× 270) showing the firm attachment of the basal cell layer to the cutis.

2. Gentle rubbing of the surface of the skin (area D) caused a loss of the superficial layers of the epidermis (Nikolsky sign).

3. After gentle stroking in a predisposed site (D, 1 hour) a vesicle appeared within one hour. The epidermal cells became more rounded, lost their prickles and had an alteration of their tinctorial properties. The picture at first glance suggested that of dyskeratosis, but closer examination revealed no *corps ronds* or other changes seen in an accelerated dyskeratotic process. The same sequence of events appeared after even the slight trauma of excising tissue (area A). The process in both areas (A and D) seemed to reach its maximum in from three to five hours.

4. Tissue removed from a site that had never been previously involved (area C) revealed no abnormalities.

5. Stroking of this same site (area C) did not produce any microscopic changes in contrast to the changes that were seen in previously involved areas.

6. The roentgen rays that were given were not responsible for the pathologic changes noted. This was demonstrated by the similarity of the picture seen in areas which had not received much roentgen irradiation (areas A and D) as compared with sites already showing signs of sequelae of roentgen irradiation (area B).

7. Lesions of three hours' duration (D, 3 hours) and three months' duration (case 2) presented essentially the same microscopic picture: epidermal vesicles and changes in the epidermal cells. However, no *corps ronds* were seen even in the older lesions.

8. Lesions that were produced experimentally had the same microscopic picture as those that appeared under ordinary circumstances.

9. Sites of predilection as observed in this study showed an absence of elastic tissue in the upper portion of the cutis.

CLINICAL FEATURES

The history and clinical appearance in the cases herein described were strikingly similar to those seen in the patients previously described by Pels and Goodman,[1] Hailey and Hailey[2] and Ayres and Anderson.[3] The main clinical features may be summarized as follows:

1. *Family History.*—One of our patients stated that both his father and his brother had a similar eruption. The second stated that his maternal cousin had a similar eruption. No one could be discovered in the third patient's family who had this condition. All patients described by the aforementioned authors stated that other members of their families suffered from a similar cutaneous disorder. Ayres and Anderson were personally able to verify this in 3 of their 5 cases. The Hailey report contains a description of two pairs of siblings. The

patient described by Pels and Goodman stated that his father had suffered from a cutaneous disease for many years, the cause of which was unknown. The later report of Hailey and Hailey [6] and the observations of Becker and Obermayer [9] prove the familial character of this disease.

2. *Location.*—In our patients the areas of predisposition were the collar areas of the neck, the axillas, the genitocrural areas and the scrotum. All of the patients described by the aforementioned authors had a similar distribution, although in isolated instances the same type of eruption was observed involving the perianal and umbilical areas, shoulders, buttocks, nasolabial folds, extremities, eyelids and corneas.

3. *Effects of Trauma.*—An outstanding feature noted in our patients was the fact that slight irritation of a predisposed area was sufficient to produce this eruption. A similar phenomenon was noted in 3 of the patients described by Ayres and Anderson. It was possible to elicit a Nikolsky sign on the back of the neck in our patients. Hailey and Hailey were also able to demonstrate this phenomenon in their patients. However, Pels and Goodman reported that this sign was not demonstrable in their patient.

4. *Clinical Course.*—The clinical course, the duration of the individual attacks and the appearance of the eruption observed in our patients were similar to those in the previously described patients. The individual lesions invariably responded favorably to fractional doses of superficial unfiltered roentgen rays. A similar response was noted in the patients of Anderson and Ayres. Hailey and Hailey stated, however, that this form of therapy was unsatisfactory in one of their patients.

5. *Laboratory Observations.*—The results of laboratory tests performed in our cases were negative except for the phytopharmacologic tests, the results of which were in the toxic zone (44 and 43 per cent in two different determinations in case 1 and 53 per cent in case 2). In the cases reported by Hailey and Hailey the results of tests varied from "normal" to "most toxic." The patient described by Pels and Goodman also gave toxic readings, 50 and 61 per cent.

COMMENT

From the clinical appearance of this dermatosis, Ayres and Anderson [3] have pointed out, there is a morphologic resemblance to the following conditions: herpes simplex, dermatitis repens, ids, dermatitis medicamentosa and infectious eczematoid dermatitis. Also, the pemphigus groups of diseases and epidermolysis bullosa have similarities.

From the histologic point of view one feels the necessity of distinguishing this from the aforementioned entities and in addition from keratosis follicularis.

From the study of our cases and those previously reported the following uniform observations appear to be evident: 1. There is a definite history of familial occurrence. 2. There are definite sites of predilection (neck, axilla, groins, etc.). 3. There is a peculiar clinical appearance. Although it is confusing when first seen by the clinician, observation of further cases makes the clinical diagnosis evident without dependence on the histologic structure. 4. In our cases and in most of those reported, irritation plays a definite role in producing the lesions. This is further emphasized in our cases by our ability to produce lesions at the sites of predilection by slight trauma and by our failure to produce lesions by similar and more excessive trauma on other areas in the same patient.

Among the entities previously described as having suggestive clinical and pathologic appearance, none show all the characteristics that this condition presents.

We are fully aware of many similarities that would suggest a relation to pemphigus, Darier's disease and dermatitis herpetiformis, as has been suggested by other authors. However, it is our contention that there is not enough similarity to allow for such a point of view at present. The condition presents a definite clinical and microscopic picture that justifies its consideration as a separate entity until further observations are able to place it in a definite category. The rapidity of appearance of dyskeratoid cells as reported here and the clinical appearance of the lesions segregate this entity from other conditions.

It is our opinion that this condition is probably a nevoid process and that it shows greatest similarity to epidermolysis bullosa.

However, in view of the confusion that premature classification would add to this problem, we offer a neutral name that merely points out the most outstanding features of the disease.

SUMMARY

1. A dermatosis is described in which the predominant histologic features are a dyskeratosis-like process in the epidermis with the formation of epidermal vesicles. This eruption occurs in members of the same family and has definite sites of predilection.

2. Examination of tissue from areas which had previously been involved but which were apparently normal at the time of removal showed a lack of epidermal cellular cohesion and epidermal spaces and also the absence of elastic tissue in the upper portion of the cutis.

3. Serial histologic studies showed dyskeratosis-like (dyskeratoid) changes and vesicles which appeared in the epidermis within one hour after the production of a lesion by slight trauma. This process reached its maximum in three to five hours.

4. A neutral name which indicates the outstanding microscopic feature, namely, dyskeratoid dermatosis, is offered to differentiate the disease from other entities which have some similarities but not enough to justify its classification with any one of them.

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ABSTRACT OF DISCUSSION

DR. M. H. GOODMAN, Baltimore: Drs. Frank and Rein should be congratulated on having made a noteworthy contribution to the knowledge of this peculiar cutaneous disease.

I am confirmed now in the view which Dr. Pels and I expressed in our original article that this dermatosis represents a form of Darier's disease with vesiculation or bullous formation. I have already presented data which served to rule out pemphigus. When we noted histologically the characteristic features of this form of dyskeratosis, namely, the splitting of the rete cells to form fissures and lacunas, the loss of prickles, the rounding out of many of the rete cells and the hyperkeratosis, we felt that the history, the clinical features and the course of the disease all merged into a picture of a dyskeratosis similar to Darier's disease. We did not consider it to be related to epidermolysis bullosa, because clinically there is not a simple vulnerability of the skin to trauma with the appearance of lesions at sites of pressure. The subepidermal disruption or absence of elastic tissue, to which Drs. Frank and Rein referred, may in my opinion be observed in any process which includes inflammatory phenomena even of banal or of secondary type.

The age of onset of the disease was usually 16 to 18 years. Becker and Obermayer in their report of 27 cases among 78 members of a family in three generations found the dominant heredity in this bullous process to be identical with that in cases of Darier's disease. Again, as in Darier's disease, the distribution is seborrheic; the course is chronic, and there may be temporary favorable response to roentgen ray therapy. Furthermore, as Drs. Frank and Rein have noted, the primary lesion by their interpretation is an erythematous macule. This is precisely the primary lesion in Darier's disease, as was brought out in Hidaka's thorough histologic studies. Ayres and Anderson in their report mentioned papulovesicles. In our case the primary lesion was also an erythematous macule which became papular and the vesicles and bullae invariably appeared on a faintly papular base. I think it will be agreed that this does not occur in pemphigus or in epidermolysis bullosa.

Drs. Frank and Rein in 2 patients elicited a positive Nikolsky sign in the apparently normal skin of previously involved areas but not in areas which had never been involved. The authors were able to demonstrate fully developed lesions three to five hours after mechanical stroking in these previously involved (so-called predisposed) regions. Similar experiments were unsuccessful in areas remote from these. Strictly speaking, one should not consider the Nikolsky sign as positive when elicited in areas altered to such a degree as described, even if the clinical appearance is apparently normal. On the other hand, the production of lesions by mechanical friction as carried out by the authors in these predisposed regions should be viewed as examples of isomorphic responses, or as Köbner phenomena. We were able also in our case to produce lesions in lines of scratching and by friction not only at sites of predilection but even in non-predisposed areas, for example on the wrist. We agree with the authors that such provoked lesions develop rapidly to full maturity. It is this very feature of

isomorphic response to irritation (Köbner reaction) which brings the disease under discussion into close relation to Darier's disease. Bettmann in 1921 reported experiments in which he produced lesions in patients with keratosis follicularis (Darier) by means of cantharides plaster, the Pacquelin cautery and ultraviolet radiation from a water cooled quartz mercury vapor arc lamp. Bettmann's studies, in confirmation of an opinion previously expressed by Darier, suggested that a specific or peculiar inborn property of the skin in patients with Darier's disease responds to trauma by way of changes specifically characteristic.

Finally, to reconcile the scarcity or absence of *corps ronds* and *grains* in the disease under discussion with the opinion of Dr. Pels and myself that it represents a form of Darier's dyskeratosis, one must invoke a fundamental phenomenon which is inherent in the latter disease. Brünauer has emphasized the fact that there is often noted in sections from lesions of Darier's disease a proliferative process in the basal layer which may be of such degree as to suggest epitheliomatous growth. Our studies of the disease under discussion seem to indicate that this aspect of Darier's disease, namely, a hyperplasia of the basal cells, is its most prominent feature. In brief, we are inclined to the conclusion that in Darier's disease, in addition to *corps ronds* and *grains*, a fundamental phenomenon of dyskeratosis is the formation of cells of the basal type which are deficient in the properties necessary to produce normal prickle cells. Since these cells are devoid of spinous processes, fluid rapidly collects in the potential spaces between them and the fissures, and lacunas result which are seen in prepared and stained microscopic sections. These basal-like cells form rapidly and early and therefore probably account for the full development of a provoked lesion within three to five hours in the experiments of Drs. Frank and Rein. It would seem that in this process just as in Darier's disease the genetic dystrophy of the basal cells is expressed in a speeding up or slowing down of the function of the basal cells in their production of prickle cells.

I have here a slide from another case, that of a woman aged 52 at the time of examination who stated that she had lesions for about four months. Dr. Ellis first encountered this case in the clinic of the Johns Hopkins Hospital. The typical process, that is, the fissures and lacunas, are seen. There is some hyperkeratosis; parakeratosis is very rare or absent. There is some rounding out of the cells to suggest *corps ronds*, but the cells are not typical ones. Of course no *grains* are found. There are foci to be seen—not so clearly on this slide—foci which are composed of hyperplastic basal cells.

In another slide from the same case, stained for elastic tissue, I was not able to find any distinct disruption or absence of elastic tissue in the subepidermal region. In the subepidermal region well preserved strands of elastic tissue were present. In other words, I was unable in these cases to find any change from the normal in the elastic tissue.

Dr. Nelson Paul Anderson, Los Angeles: The birth of any new and independent dermatologic entity is generally attended by considerable travail. The truth of this statement is indicated by the fact that six different names have been given to this new foundling. In 1938 Pels and Goodman undoubtedly described this entity as a vesicular variant of Darier's disease. A short time later Hailey and Hailey made the designation of familial benign chronic pemphigus. This was followed by the recurrent herpetiform dermatitis repens of Ayres and Anderson. Familial benign chronic bullous dermatosis was the term used by Franks and Traub. Becker suggested the term dyskeratosis bullosa hereditaria. And, finally, Drs. Frank and Rein, the presenters of today's excellent paper, have suggested the appelation dyskeratoid dermatosis.

In this discussion, I shall avoid the dreadful mire of dermatologic nomenclature, which after all is only an attempt to group or classify cutaneous diseases, and shall restrict my remarks to an attempt to answer the question, "Is this a true and independent disease entity?"

From a clinical standpoint, the answer must be the affirmative. The following clinical characteristics support this assertion:

1. The areas involved—the topographic distribution of the eruption—are practically the same in all the reported cases. These areas are the collar region of the neck, the axillas, the groins and the perianal regions.

2. The striking familial or hereditary features of the disease were present in both patients of Drs. Frank and Rein, in the cases of Hailey and Hailey, who were the first to include such a tendency in the name which they gave the disease, namely, familial benign pemphigus, in several of the patients described by Drs. Ayres and myself, in the 2 cases of Franks and Traub and, above all, in the series of 27 cases among 78 persons in three generations reported by Becker and Obermayer.

3. The cutaneous lesions themselves, in my opinion, present certain morphologic characteristics sufficient to differentiate them from any previously described entity. In fact, the photographs published by those who have written on this disease are strikingly similar. The primary change, as shown by the experimental reproduction of the disease by Drs. Frank and Rein, is an erythematous macule which rapidly becomes vesicular. This vesicular phase spreads peripherally in a manner that suggests an undermining of the epidermis but which histologically is seen to be cleavage within the epidermis itself. Eventually there are produced erythematous patches composed of isolated and coalesced vesicles, especially pronounced at the periphery of the lesion. As the development progresses, further central involution occurs, and there is seen a peculiar wrinkling or crinkling of the skin suggesting a pseudoatrophy. As the thin-walled vesicles easily rupture, yellowish brown impetiginous-like crusts are formed. The entire process finally resolved, leaving a temporarily pigmented patch.

4. The ready elicitation of Nikolsky's sign in practically all of the cases in which it has been attempted is also a clinical feature of note.

5. The chronic course of this entity, lasting in some cases for at least twenty years, with intermissions and exacerbations, is striking. Finally, the benign course during all of the reported cases is also noteworthy.

The microscopic observations in both the early and the late lesions of this disease are characteristic. This somewhat dogmatic assertion was first made by myself in discussing a case of this disease presented before the Los Angeles Dermatological Society (ARCH. DERMAT. & SYPH. **42**:491 [Sept.] 1940). Today after the histologic study of several additional cases and a fairly thorough review of the histologic observations in all of the reported cases, including those of Pels and Goodman, I am more than ever convinced of the correctness of the assertion. It is extremely interesting in this connection to note that in case 2 of Drs. Frank and Rein the condition was correctly diagnosed by Dr. Wilbert Sachs from a histologic section, from which an entirely different diagnosis had been originally made. Only then was the patient again seen and the true nature of the disease determined. I am in complete accord with both the observations and their interpretation of Drs. Frank and Rein. In view of the early publication of Pels and Goodman and their insistence that the condition in their case was a variant of Darier's disease, it is extremely interesting to note that none of the subsequent authors dealing with this entity have felt that this diagnosis was tenable either clinically or histologically.

DR. M. E. OBERMAYER, Chicago: I should like to state that this interesting clinical entity presented by Drs. Frank and Rein is not always familial. At the University of Chicago clinics I have under observation a patient whose case is as yet unreported. No history of a similar cutaneous disease in the patient's family could be elicited. It seems, therefore, that present day concepts of the disease will have to be revised.

As to the term used by the authors, I agree with Dr. Becker that dyskeratosis bullosa would be a more logical term. The histologic features are not dyskeratoid but are those of true dyskeratosis.

DR. F. A. ELLIS, Baltimore: I wish to go on record calling this particular syndrome a variant of Darier's disease. At least, the condition in many of the cases that have been presented was a form of Darier's disease. I have a biopsy specimen from one of the 2 brothers reported in the original series by Hailey and Hailey.[2] The sections showed *corps ronds,* and the histologic diagnosis was Darier's disease.

In the patient described in the discussion by Dr. Goodman the lesion had been present for several weeks; it had rapidly enlarged with clearing in the center forming annular lesions. The eruption disappeared completely after the taking of tissue for biopsy under the boric acid ointment dressings. There were *corps ronds* present but no *grains.*

Attention is called to the series of cases of familial Darier's disease reported by Hitch, Calloway and Moseley (*South. M. J.* **34**:578 [June] 1941). They observed 14 cases in one family; 40 per cent of the females were affected. The predominating lesion was on the neck and had originally been diagnosed seborrheic dermatitis.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I had the opportunity of studying the histologic changes in the first 2 cases of the Drs. Hailey, and since then I have seen sections from about 6 additional cases, including one of Dr. Becker's. The pathologic diagnoses raised have always been a question of Darier's disease, dermatitis herpetiformis and pemphigus. In the photomicrograph shown today there were certain cells that might have been designated as *corps ronds;* I did not see any *grains.* The formation of lacunas and intraepidermal spaces and the general arrangement of dyskeratotic cells were not what one usually sees in Darier's disease. In other cases of the condition that the presenters described and which I believe to be an entity I have been unwilling to make a pathologic diagnosis of Darier's disease. The presence of occasional *corps ronds,* which is a benign type of dyskeratotic cell that has undergone partial keratinization and has lost its prickles, does not in itself make a diagnosis of Darier's disease, as there are many other conditions in which occasional *corps ronds* are to be found. The histologic picture is too inflammatory for pemphigus. I have not seen any proliferation of basal cells such as Goodman has emphasized. Dr. Sachs is to be commended for making a microscopic diagnosis; but after observing a few cases of this kind one learns to suspect the microscopic diagnosis, if only because the histologic picture does not quite fit in with any of the conditions which the disease under consideration simulates. I agree with Dr. Anderson and the other discussers that the condition under consideration is a definite clinical entity. Personally, I think the name suggested by Drs. Becker and Obermayer is the best of the whole group of names used in describing this condition.

DR. FRED D. WEIDMAN, Philadelphia: I became involved in this controversy early in its history. While the Drs. Hailey were studying their cases, slides were

sent to me, among others, and I am afraid that I am responsible for the use of the term pemphigus. I want to apologize for that; at that time I did not realize that the condition was going to get the publicity that it did, and I really suggested the term pemphigus simply to get away from the idea that the condition was Darier's disease; that is, it was a stopgap term.

It was particularly cheering to me in this presentation by Drs. Frank and Rein to note something which I think is eminently to be desired. As I have said two or three times during this meeting, the features of the condition should be studied at various stages of its development. The authors have done that very thing. They have secured one of the earliest lesions that one can imagine and conducted histologic studies on it when it was only a few hours old. By doing that, they have rendered a service by showing what the nature of the primary fundamental process was. They have shown that it is primarily a vesicular condition, unlike Darier's disease. Darier's disease, if nothing else, is fundamentally and predominantly keratotic, as witness the original name, dyskeratosis follicularis.

In the sections of the Drs. Hailey that I saw there was not anything that appealed to me as being dyskeratotic. The cells in question were degenerative, it is true; but simple degeneration does not spell dyskeratosis. If one looks at the margins of a vesicle of varicella, even, one can see cells that are similar indeed to ones in this dermatosis of the Haileys. But they are only degenerations. In this discussion nobody has been satisfied that the cellular changes are clearcut dyskeratosis. There is an approach to it—yes—but not a genuine dyskeratosis.

Now, no matter how early the lesion is examined in Darier's disease, one will always find dyskeratosis, together with definite plugs of keratotic material. As the disease was originally predicated by Darier on the basis of this outstanding dyskeratotic feature, I think that it is a mistake to force the Haileys' dermatosis into a particular niche by trying to alter the concept of Darier's disease.

In short, I am on the side of those who favor the concept that this condition is something definitely distinct from Darier's disease. I am not going to step into the matter of nomenclature. If anything, I should prefer to call the disease the Haileys' dermatosis and let it go at that. What would have happened, for example, if in the earlier history of disease of the kidney, with knowledge as scant as it was, renal disease had started out with some pretentious name, acute, chronic, parenchymatous and interstitial and all that? The physicans of that day simply called it Bright's disease. Only when the real nature of the condition was determined later and a proper basis had been secured for advancing a really descriptive nomenclature did such names as glomerulonephritis come into the picture. Accordingly, I am going to propose another name for the disease under discussion, namely, the Haileys' dermatosis.

Dr. Charles R. Rein, New York: Dr. Obermayer has observed that this condition is not always familial. We agree with this observation, since in one of our patients there was no familial history of a similar eruption.

Dr. Weidman referred to the fact that the peculiar cells found in this condition "approach dyskeratosis." It is our belief that they are not true dyskeratotic cells, as seen in the characteristic dyskeratotic dermatoses. Further detailed histologic and cytologic studies may determine whether this condition is a true dyskeratosis or a dyskeratosis-like (dyskeratoid) dermatosis.

A point of great interest is the fact that the clinical picture and the characteristic microscopic observations can be produced in less than three hours in the apparently normal skin of patients with this disease by mild trauma.

We agree with the many investigators who now feel that this condition is in no way related to pemphigus, Darier's disease or Duhring's disease.

Clinical Notes

DERMATITIS DUE TO LIQUID LIP ROUGE

IRVING L. SCHONBERG, M.D., CLEVELAND

A new item has been added to the already overflowing stock on the cosmetic counter. With its arrival numerous reports of hypersensitivity may be anticipated. Liquid lip rouge is a red liquid, somewhat lighter in consistency than nail polish. Its justification for existence is based on the facts that it will not

Erythematovesicular dermatitis of the face and arm due to liquid lip rouge.

smear and that one application usually suffices for the day. The following report is of a severe dermatitis resulting from the use of a liquid rouge.

REPORT OF A CASE

S. R., a white girl aged 19, had been using liquid lip rouge for the past two weeks. On July 19, 1941 she noticed slight swelling of both lips. This was accompanied by burning and itching. Later that same day small white blisters appeared on the lips. She discontinued the application of the lip rouge. The following day redness and swelling developed over the entire face. Blisters developed on the tongue. On the following day erythematous patches and vesicles involving the neck and the right arm appeared. The patch on the right arm was approximately the size of the lips. She stated that she had a habit of sleeping on her right arm.

Examination on July 22 showed an acute vesicular eruption on the cheeks, nose, lips and angles of the jaw. The lesions were pinhead-sized vesicles and

erythematous macules. The lips were edematous, and an exudative vesicular process was present. There were numerous deep fissures and a considerable number of yellowish crusts on the lips. On the right arm there were two erythematous scaly patches approximating the shape of the lips. There were a few vesicles on the tongue. The conjunctiva of the lids was injected. There were grouped vesicular patches on the neck.

The site of a patch test with the liquid lip rouge became edematous and vesicular in twenty-four hours, later becoming a large pea-sized bulla.

Treatment consisted of wet dressings of solution of aluminum acetate N. F., borated cold cream and subfractional doses of roentgen rays.

524 Keith Building.

A NEW EMULSION TYPE OF HAND LOTION FOR DERMATOLOGIC USE

ARTHUR E. SCHILLER, M.D., DETROIT

A search of the literature shows that the majority of the emulsion type lotions in the past have contained tragacanth, acacia or quince. These lotions all have a tendency to change in character and to break down on the addition of various medicaments. The following formula is for a lotion which is made with wetting agents of the new type, triethanolamine and cetyl alcohol, and is, I believe, peculiarly adapted to dermatologic use:

Stearic acid	1.75 Gm.
Glycerin	1.00 cc.
Cholesterol base	0.50 Gm.
Cetyl alcohol	0.50 Gm.
Triethanolamine	0.15 cc.
15 per cent alcohol, in sufficient quantity to make	100.00 cc.

Directions: Allow the stearic acid and the triethanolamine to react for twenty minutes, or until the reaction is complete. Add the cholesterol base, cetyl alcohol and glycerin (which must have been brought to the same temperature as the other components), and when this mixture is melted gradually stir in the 15 per cent alcohol (which also has been warmed to the same temperature). Stir or agitate until cool. Perfume as desired.

The value of this formula is that the emulsion is permanent and shows no tendency to break down. It is free of quince, tragacanth and acacia and is not tacky. All of the ingredients can be sterilized before the compound is made up. It will take a variety of powders, such as calamine, zinc oxide and kaolin; acids, such as phenol, salicylic acid and boric acid, and any of the alkalis within reason.

In recent years there have been presented a number of formulas making use of the new emulsifying agents, principally triethanolamine. Cetyl alcohol up to approximately 2 per cent has been found to improve emulsions of both the water in oil and the oil in water type. It has the ability to become hydrated and to assist the hydration of other components and in this way increases the stability of the lotion. In addition, it has a tendency to leave the skin smooth. The oil in the lotion is furnished by the cholesterol base.

This lotion was suggested to me by Prof. Gordon A. Bergey, professor of pharmacy, West Virginia University, and I have found it one of the best I have ever used.

10 Peterboro Street.

Correspondence

DERMATITIS ATROPHICANS LIPOIDES DIABETICA; NECROBIOSIS LIPOIDICA DIABETICORUM

To the Editor:—Since there are confusing statements in the older literature about the historical facts pertaining to dermatitis atrophicans lipoides diabetica, or necrobiosis lipoidica diabeticorum, we should like to state the following points:

Maurice Oppenheim presented a case under the designation "Eigentümliche disseminierte Degeneration des Bindegewebes der Haut bei einem Diabetiker" before the Viennese Dermatological Society on June 20, 1929 (*Zentralbl. f. Haut- u. Geschlechtskr.* **32**:179, 1930) and again on June 26, 1930 under the name "Eigentümliche Bindegewebsdegeneration" (ibid. **36**:162, 1931). The presentation of this case included a complete and detailed account of the clinical picture and the clinical course of this new disease. Oppenheim also gave a detailed histologic description on the occasion of these two presentations with a demonstration of the histologic observations but without a report on fat.

Two and one-half years later, on Jan. 14, 1932, at a meeting of the Viennese Dermatological Society, Erich Urbach presented a woman with the diagnosis "Multiple degenerative Gewebsschädigungen der Haut mit extracellulären Lipoideinlagerungen bei einem Fall von schweren Diabetes" (*Zentralbl. f. Haut- u. Geschlechtskr.* **41**:422, 1932). On Feb. 11, 1932 Urbach presented his case again and gave the disease the name necrobiosis lipoidica diabetica on the basis of his observations regarding the lipoid imbibition of the tissue. In the discussion Oppenheim suggested the term dermatitis atrophicans lipoides diabetica. The latter presented his case under the same name with a detailed clinical and histologic description at a meeting of Die Gesellschaft der Aerzte in Vienna on Feb. 6, 1932 (*Wien. klin. Wchnschr.* **45**:314, 1932). A full description of this entity was published by Urbach with the name necrobiosis lipoidica diabeticorum (*Arch. f. Dermat. u. Syph.* **166**:273, 1932). Oppenheim published a full paper on this new disease with the title "Über eine bisher nicht beschriebene, mit eigentümlicher lipoider Degeneration der Elastica und des Bindegewebes einhergehende chronische Dermatose bei Diabetes mellitus" in the same volume (p. 576).

From these facts it can be seen that Oppenheim has priority in the clinical and histologic description of the disease and its connection with diabetes except for the description of its lipoid character. Urbach has priority in establishing the pathogenesis that this disease is one of the localized cutaneous lipoidoses.

MAURICE OPPENHEIM, M.D., Chicago.
ERICH URBACH, M.D., Philadelphia.

WETTING AGENTS AND POSSIBLE DANGER FROM THEIR USE

To the Editor:—At the session of the American Academy of Dermatology and Syphilology just concluded (December 1941, New York) abundant consideration was given to wetting agents, their nature and uses. I fear, however, that one possible effect of their use was entirely ignored. I refer to their influence on the character of keratin (surface of the skin) as a permeable membrane. One seeks to maintain for the cutaneous surface a high degree of impermeability (protective surface); yet it has been demonstrated that use of wetting agents in the compounding of topical mixtures has influenced its permeability profoundly.

I have demonstrated that the oleoresinous irritant in rhus can be extracted as effectively with "wetted" water as with acetone and has the same irritative index for skin as has the latter. Colleagues working with the same principle are rendering the skin completely permeable to many complex substances, including common allergens.

While it is understandable that a therapeutic mixture to be used on diseased skin for a specific purpose and for a limited time should increase the penetrability of the skin for the therapeutic agent, the habitual use of wetting agents as cleansers of the skin in place of soap is fraught with dangerous possibilities. Before the use of wetting agents as cleansers receives unqualified endorsement, the significance of the hazard herein mentioned should be definitely determined.

HERMAN SHARLIT, M.D., New York.

News and Comment

MILITARY SERVICES OF MEDICAL STUDENTS, INTERNS AND RESIDENTS

The Association of American Medical Colleges has cooperated with National Headquarters of the Selective Service System and with the Surgeon General of the Army and the Surgeon General of the Navy in a plan designed to "persuade" all third and fourth year medical students who are physically and otherwise eligible to join the Medical Corps Reserve of either the Army or the Navy. The Army is in need of more medical officers for the present forces. The immediate needs of the Navy are less urgent, but there will be a call for more medical officers as its forces are enlarged.

Each fourth year medical student in the Medical Administration Corps Reserve should apply for a commission in the Medical Corps Reserve within twelve months after graduation from medical school. Each student in the Naval Reserve should apply about three months before graduation for a commission in the Medical Corps Reserve of the Navy. It is expected that each student will be permitted to complete an internship of at least one year.

The Association has adopted a policy that all third and fourth year students be urged to apply for a commission in the Medical Administration Corps Reserve or in the Naval Reserve and that the deans of the medical schools henceforth refuse to support the request of students for further deferment under the Selective Service until they have applied for a commission in either the Medical Administration Corps Reserve or the Naval Reserve if they are physically and otherwise eligible for such commissions. There then would be the choice of either joining one of the reserves or being subject to induction as a private.

A somewhat similar situation pertains to interns, fellows and residents. Even though they have been deferred by Selective Service in order to complete their training or to maintain the essential services they are rendering in the local communities, these persons are not inductable after June 30 following their twenty-eighth birthday. A considerable number of such young men have taken advantage of this situation and have not accepted commissions and have not carried out the implied obligation of their deferment. It has therefore been proposed by Selective Service that the deferment of all interns, residents and fellows be discontinued for those who are eligible for a commission in the Medical Corps Reserve of either the Army or the Navy.

The Surgeon General of the Army has agreed to appoint an Advisory Committee to each of the Corps Area Surgeons comprising representatives of the medical schools, of the hospitals and of the medical profession of that area. The proposed Advisory Committees would advise the Corps Area Surgeon in calling to duty the reserve officers in such a way that their withdrawal from the hospitals and other institutions would interfere least with the services which those institutions are rendering to their local communities or that would impose as little handicap as possible in the continued training of these young men in the various specialties. As far as practicable, residents in hospitals approved for graduate education will be permitted to complete preparation for their specialty. All concerned recognize that the military as well as the civilian needs for specialists should be given full consideration.

As an inducement for young physicians to take commissions, the Surgeon General of the Army has recommended to the General Staff that promotion in the Medical Corps by selection be put into effect. If this is approved, medical corps officers with special qualifications will be given rank higher than that of First Lieutenant. This request has not at present been approved.

MILITARY AND NAVAL SERVICE FOR MEDICAL STUDENTS AND INTERNS

The following memorandum has recently been issued to deans of medical schools by the national headquarters of the Selective Service System:

"Both the Army and the Navy have adopted a policy under which commissions may be granted to qualified third and fourth year medical students enrolled in acceptable medical schools. When so commissioned, such men will be permitted to complete their medical training, including one year of internship, before being ordered to active duty.

"Local boards should, therefore, advise all third and fourth year medical students and first year internes who come before them for classification that they may make application for commissions in either of the services. Registrants so applying should be deferred pursuant to the provisions of Memorandum to All State Directors, 1-18, pending receipt of their commissions.

"The classification of third and fourth year medical students and internes who have been classified in Class II-A and who refuse to apply for a commission in one of the services may be reconsidered by the local board, and such persons, if not otherwise deferred and if found physically qualified, may be classified in Class I-A. Third and fourth year medical students and internes who are rejected after applying for commissions may be classified pursuant to the provisions of Memorandum to All State Directors, I-91. First and second year medical students and those who have been accepted as students in a medical school may be classified as heretofore pursuant to the provisions of Memorandum to All State Directors, I-91."

SOCIAL HYGIENE

The sixth National Social Hygiene Day, one of America's leading public health events, will be observed on Wednesday, Feb. 4, 1942, with the theme "Keep America strong, help build better health." This year's Social Hygiene Day is directing special attention toward the full realization of the menace of organized prostitution in areas adjacent to concentrations of armed forces and in industrial centers.

Stating that physical fitness of military men and defense workers will be among the important factors in determining the effectiveness of the country's defense effort, Dr. Ray Lyman Wilbur warned America that the nation's defense also depends on a healthy civilian population.

"The good work begun in national control will be cancelled, the declining attack rate of syphilis and gonorrhea will be swiftly reversed, unless to our concern with munitions and maneuvers and equipment we add specific attention to the protection of our men in the armed forces and in the factories which supply our materials," Dr. Wilbur said.

"That age-old institution the 'red-light district' is not the only factor with which venereal disease control officers and law enforcement authorities have to contend. Within the past decade, the mushroom growth of the 'honky-tonk,' the

roadside cabin, and the roving operator whose activities are abetted greatly by the development of modern transportation, have all combined to complicate the problem.

"The repression of prostitution is a civilian community problem and one over which military authorities ordinarily have no direct control. Therefore, an effective solution of this problem will depend upon strict enforcement by the police of existing laws dealing with the practice of prostitution. The prostitute is the usual human carrier of the spirochete of syphilis and the gonococcus. Every effort should be made to make her difficult to meet. Every contact is a danger. The fewer contacts the fewer wasted lives. Enforcement of the laws that can protect your youth requires a responsible public opinion to back up police officials. In addition, such law enforcement must not merely be concerned with the activities of prostitutes themselves, but must as well extend to the owners and operators of bawdy houses, disreputable hotels, tourist camps, and 'honky tonks,' where open or commercialized prostitution is tolerated."

Information concerning Social Hygiene Day may be obtained by writing to the American Social Hygiene Association, 1790 Broadway, New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

At the meeting of the American Board of Dermatology and Syphilology in New York on Dec. 12 and 13, 1941, 69 candidates were considered. Fifty-four were awarded the certificate of the board, while 15 did not qualify. Including the diplomates certified at this meeting, there have been 670 physicians certified. Since the board has been in operation, 720 applications have been received.

The survey of graduate training in dermatology and syphilology has been practically completed. The questionnaires of all the institutions with graduates in training for this specialty have been reviewed, and only a few questionnaires now remain to be considered by the board and by the Council on Medical Education and Hospitals of the American Medical Association.

The matter of preceptors for graduate students in training has been considered during the past year, and blanks for applicants to act as preceptors for students in training in dermatology and syphilology have been prepared and are ready for distribution.

It has been decided to obtain from chiefs of clinics annual reports of all students in training, so that such reports will be available when the applications of these students will be considered for certification by the board.

During the past year the board has participated actively with the Committee on Medical Preparedness of the American Medical Association in a survey of physicians throughout the country.

The syllabus on graduate training has been reviewed, and a new issue of this booklet is now being considered.

A complete list of the diplomates of the board, including those certified at the recent meeting, will appear in the new edition of the Directory of Medical Specialists, which will be published in the early part of 1942. This book will contain some 4,000 new names of the diplomates of the boards. This directory can be obtained from the Columbia University Press, New York.

The Board decided at the recent meeting that in order to qualify for the oral examination all candidates in group B must previously pass the written examination.

The following applicants were certified at the last meeting of the Board:

Harry L. Arnold Jr., Honolulu, Territory of Hawaii; Tibór Benedek, Chicago; Alex D. Campbell, Seattle; John G. Copeland, Albany, N. Y.; Louis Dantzig, New York; Marion I. Davis, Nashville, Tenn.; Douglass A. Decker, Allentown, Pa.; Gerard A. De Oreo, Fort Thomas, Ky.; Earl L. Eaton, Buffalo; Richard Emmet, Brooklyn; Martin F. Engman Jr., St. Louis; Harry B. Feiler, New York; William Garbe, Toronto, Canada; Arthur W. Glick, New York; Hugh E. Hailey, Atlanta, Ga.; William R. Hill Jr., Boston; Jacob H. Hirsch, Haverstraw. N. Y.; Irving N. Holtzman, Brooklyn; Isidor Kaminstein, Jamaica, N. Y.; Richard J. Kelly, New York; Charles B. Kennedy, New Orleans; Solomon A. Klein, New York; Robert R. Kierland, Rochester, Minn.; Frank J. Lacksen, Columbus, Ohio; Walter F. Lever, Boston; Clarence S. Livingood, Philadelphia; Mary M. Man, New York; Morris D. Marcus, St. Louis; Leonard S. Markson, Milwaukee; Harold L. Miller, Milwaukee; Harry Pariser, Philadelphia; Nathan Pensky, Brooklyn; Isidore Pincus, New York; Shepard Quinby, Buffalo; Leon F. Ray, Portland, Ore.; Paul G. Reque, Durham, N. C.; Morris M. Reschke, New York; Robert J. Reuter, Milwaukee; Cornelia F. Robertson, New York; Francesco Ronchese, Providence, R. I.; Albert Rubin, Brooklyn; Morris H. Saffron, Passaic, N. J.; Harry Sklar, Hempstead, N. Y.; Albert H. Slepyan, Chicago; James S. Snow, Birmingham, Ala.; Lauren McC. Sompayrac, Jacksonville, Fla.; Charles D. Stewart, Corpus Christi, Texas; William B. Swarts, Greenwich, Conn.; Herbert L. Traenkle, Schenectady, N. Y.; Harold R. Vogel, Pittsburgh; Leon H. Warren, Bethesda, Md.; Harry W. Woolhandler, Chicago; Sadie Zaidens, New York, and Israel Zeligman, Baltimore.

Obituaries

AUGUSTO DUCREY

Augusto Ducrey was born in Naples, Italy, of a Swiss father and a Neapolitan mother. He received his premedical and medical education in his native city, obtaining prizes and diplomas of merit. Particularly interested in histopathology and bacteriology and then in dermatology, he did most of his brilliant work on the soft chancre under the guidance of Tommaso De Amicis, being his assistant between 1884 and 1894.

The discovery of the streptobacillus bearing his name, at first not appreciated and much discussed and then universally recognized, gave him a well deserved reputation.

First professor of dermatology in the University of Pisa, then in Genoa and finally in Rome, he ended his fruitful life in Rome at the age of 80.

His contribution to the field of dermatology is more in quality than in quantity. It was not by chance that he discovered the streptobacillus but by a simple method of progressive purification of experimental soft chancres.

Abstract of an obituary by J. CAPPELLI in *Dermosifilografo* (**16**:237, 1941).

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THERAPEUTIC METHODS IN NEUROSYPHILIS. C. L. CARLISLE and U. S. BOWEN, M. Bull. Vet. Admin. **17**:125 (Oct.) 1940. SOBISMINOL MASS IN THE TREATMENT OF SYPHILIS. E. A. MCCLINTOCK, ibid. **17**:129 (Oct.) 1940. OPTIC NERVE DAMAGE IN LUETIC PATIENTS, C. E. JOHNSON, ibid. **17**:133 (Oct.) 1940.

The efficacy of chemotherapy, particularly with sobisminol mass, developed by Hanzlik, following hyperpyrexia for the treatment of neurosyphilis is discussed by Carlisle and Bowen, by McClintock and by Johnson. Carlisle and Bowen point out that hyperpyrexia induced by malaria or short wave diathermy should be complemented by chemotherapy, as it is unlikely that pyrexial therapy, causing temperatures ranging from 104 to 107.6 F., will uniformly and for long enough heat all the tissue of the body to this spirocheticidal point. Therefore they believe that chemotherapy should take care of any spirochetes which escape the spirocheticidal effects of the heat. For this McClintock believes that oral administration of sobisminol mass is indicated, as the daily urinary bismuth excretion level of from 3 to 5 mg. necessary for effective spirochetal destruction is easily maintained by its continued administration. This has been shown by various investigators. This level of excretion was easily maintained for the 4 patients treated at the Veterans Administration Facility at Palo Alto, Calif., by the daily oral administration of 900 mg. of sobisminol mass for as long as eight weeks. Mild toxic symptoms, such as nausea, vomiting, grip, stomatitis, anorexia and a bismuth line, do occur but did not in these patients. However, the toxicity is immediately relieved when administration of the drug is discontinued. Because of toxic symptoms treatment with sobisminol mass had to be discontinued permanently with 4 and temporarily with 7 of 90 patients treated by Scholtz, McEachern and Wood. Johnson discusses the incidence of damage to the optic nerves and toxic amblyopia as by-effects of tryparsamide treatment of patients with neurosyphilis. He recommends routine ophthalmologic examination of the neurosyphilitic patient on admission to the hospital, as the results will make subsequent comparisons possible. It has been stated by Moore that if any visual impairment is to occur it will appear by or before the fifth weekly injection of tryparsamide. If no impairment is apparent by the twelfth injection the drug may thereafter be administered with impunity. All patients should be cautioned to report any visual disturbance following tryparsamide therapy. Regardless of how psychotic the patient may be, any report of a visual change should be heeded and acted on immediately. At this time probably no changes will be apparent in the disk head provided treatment (hyperpyrexia and chemotherapy) for neurosyphilis was instituted fairly early. Changes in the visual fields must now be relied on; if they are present, by discontinuing the administration of tryparsamide it is usually possible to arrest the optic process.

J. A. M. A.

AID TO DIAGNOSIS OF LATENT SYPHILIS-LUETISM. W. S. BAINBRIDGE, Mil. Surgeon **88**:492 (May) 1941.

In certain cases of syphilis the symptoms are so indefinite and generalized that they may not be of any diagnostic value and together with negative serologic reactions may lead the clinician astray. As a diagnostic adjunct, Bainbridge suggests roentgen ray examination of the hands in an effort to determine if there are any areas of budding and resorption and other changes along the shafts of the phalanges, as he considers these suggestive. He is of the opinion that even

with negative serologic reactions patients who are in a doubtful category should be given the therapeutic test for confirmation or rejection of the tentative diagnosis of syphilis.

COOMBER, Chicago.

ROSEOLA INFANTUM (EXANTHEM SUBITUM). ROY M. GREENTHAL, Wisconsin M. J. **40**:25 (Jan.) 1941.

The disease was first described in 1910, and the description of the blood picture, with its diagnostic significance, was added in 1921. Roseola infantum, often confused with other exanthems, starts abruptly with a high temperature and no abnormal physical findings. There is a relative lymphocytosis. When the temperature drops, more often on the third day, within a few hours a measles-like maculopapular rash occurs, which lasts about two days.

Most observers consider roseola infantum a clinical entity possibly due to a virus.

The author summarizes the salient points in 100 cases observed during the past five years, in which the condition conformed generally to the picture described. Ninety-five per cent of the patients were under 5 years of age. There was no seasonal incidence and no epidemic grouping. Six per cent had initial convulsions, but in general toxic symptoms were lacking. There were no complications. The lymphocytosis in about 70 per cent of the cases is the point most emphasized by the author.

JANNEY, Wauwatosa, Wis. [AM. J. DIS. CHILD.]

PIGMENTATION AND TRANSPLANTATION. ALFRED FESSLER, Brit. J. Dermat. **53**:201 (July) 1941.

One hundred and nine sections of the skin of spotted guinea pigs, 3 to 4 mm. in diameter, comprising epidermis and superficial cutis, were removed by a cutaneous punch and autotransplanted into defects products in the same way. When black skin was implanted into nonpigmented skin, extension of the area of pigmentation was visible in three weeks, and a pigmented area up to 25 mm. in diameter formed in two years, after which extension of areas of pigmentation ceased. The hairs in the region usually remained white. Brown skin implanted into white tended to show a slower extension of pigmentation, which ceased after six months. White skin implanted into black or brown skin was eventually replaced by a pigmented scar. Sections from newly pigmented areas produced extension when transplanted into nonpigmented skin. The author concludes that melanoblasts have superregenerative powers as contrasted to nonpigmented epidermal cells. He explains this power as probably being due to the presence of the specific pigment-producing oxidase and states that the high degree of malignancy of melanoma can probably be attributed to this property.

NAEVUS SEBACEUS AND SEBACEOUS CARCINOMA. LOUIS SAVATARD, Brit. J. Dermat. **53**:214 (July) 1941.

Four tumors are described of which a diagnosis of epithelioma of the sebaceous glands was made only after microscopic examination. The age and sex of the patients and the location and duration of the tumors were: a man aged 66, right temple, eighteen months; a woman aged 67, occipital region, twelve months; a man aged 68, right cheek, twelve months, and a woman aged 58, temporal region, six months. Microscopically, the point of origin was either from the surface epithelium or from basal cells of the sebaceous glands or both. A variable percentage of sebaceous gland cells were found in the tumors. In no case did the tumor originate from glands comprising naevus sebaceus.

BECKER, Chicago.

A CASE OF PROGRESSIVE SCLERODERMA WITH ASSOCIATED VITILIGO. E. DEGLOS and F. SAINT-GIRONS, Bull. Soc. pédiat. de Paris **37**:333 (June) 1939.

A girl 11½ years old had areas of pigmentation and scleroderma with intervening spots of vitiligo. The cholesterol content of the blood was slightly increased,

and the phosphatase content was high. Various organic extracts were administered, but these did not stay the development of new patches of scleroderma.

BAZIN'S INDURATED ERYTHEMA: PROBABLE ENDOCRINE ORIGIN. B. WEILL-HALLÉ and A. ABAZA, Bull. Soc. pédiat. de Paris **37**:344 (June) 1939.

A girl 15½ years old had indurated erythema on the calves of the legs. The condition had been present for four months but cleared up after six weeks of administration of thyroid. The reaction to a tuberculin test was negative. She had received BCG vaccine subcutaneously two years previously and had a weak positive tuberculin reaction about four months thereafter. Roentgenologic examination of the chest indicated nothing abnormal. A biopsy of the cutaneous lesions was not made. The lesions are regarded as tuberculids by most dermatologists. No evidence of tuberculosis was established in this case.

BENJAMIN, Montreal, Canada. [Am. J. Dis. Child.]

OCULAR MANIFESTATIONS OF LYMPHOGRANULOMA VENEREUM. VAQUEZ BARRIERE and J. MAY, Arch. de oftal. de Buenos Aires **36**:1 (Jan.) 1941.

Vaquez Barriere and May have studied the ocular symptoms produced by the virus of lymphogranuloma venereum. They confirm that there is an ocular syndrome characteristic of lymphogranuloma venereum, as was stated by Funakawa in Japan and by Luque in Chile.

In each case they have performed (*a*) a biomicroscopic examination of the conjunctiva, cornea, iris and crystalline lens, (*b*) an ophthalmoscopic examination, (*c*) a measurement of the tension of the central artery of the retina with Bailliart's ophthalmodynamometer and (*d*) a measurement of the ocular tension with Schiötz' tonometer.

The authors have examined 120 patients in different stages of lymphogranuloma venereum and some with induratio penis plastica and Dupuytren's disease, which May believes in some instances to be of lymphogranulomatous origin.

The ocular manifestations are characterized by visibility and tortuosity of abnormal nerve fibers in the central part of the retina. The optic density and the opalescence of the corneal tissue are increased. The papilla is red and flat, has hazy borders and is surrounded by grayish edema of the retina. These symptoms were observed in early and late stages of the disease. They were also observed in some controls, who later were found to have positive Frei reactions. The ocular manifestations were also present in some cases of induratio penis plastica and Dupuytren's disease.

The ocular syndrome, more or less complete, was found in 78 per cent of the patients with lymphogranuloma venereum. It was noticed as soon as fifteen days after the beginning of the primary lesion. In the inguinal type it was observed in 20 per cent of the cases.

STATISTICS OF CASES OF INDURATIO PENIS PLASTICA. J. MAY, Gac. med. d. Uruguay **2**:8 (Dec.) 1940.

For more than four years May has sustained the contention that induratio penis plastica is a sclerosis of the penis due in many cases to the virus of lymphogranuloma venereum. The author summarizes the total number of cases published in which a Frei test was performed. Up to December 1940 there were 111 cases reported in Italy, Paraguay, Japan, Spain and Uruguay. The Frei reaction was positive in 80 per cent of the cases. The ocular symptoms considered by many as characteristic of the disease were found in 22 of 30 patients (73 per cent).

INVESTIGATION OF THE PRESENCE OF SPIROCHETE CAUSING PINTA IN FIVE HUNDRED CASES. R. GOMEZ FARIAS, Rev. med. mil. **2**:32, 1939.

Gomez Farias reviews the history of different theories of causation of pinta. The mycotic theory advocated by Montoya Flores was the most popular one until

recently. The disease was also attributed to avitaminosis. Gonzales Herrejon in 1927 first suggested the theory that the disease was caused by a spirochete. The high incidence of positive Wassermann reactions was a strong argument in its favor. Saenz, Alfonso and Grau in 1938 first discovered the causative spirochete. The author performed dark field examinations in 500 cases, and in 98 per cent of them the organism was found.

CANIZARES, New York.

ANALYSIS OF BLOOD IODINE IN PATIENTS WITH CUTANEOUS DISEASES AND ITS RELATION TO THE VEGETATIVE NERVOUS SYSTEM. HERMAN BRILL and K. GOYERT, Arch. f. Dermat. u. Syph. **180**:63, 1940.

The micromethod of Leipert was used. The authors determined the iodide content of the blood of 10 control subjects (12.9 to 19.6 micrograms per hundred cubic centimeters) and 10 patients with eczema (10.7 to 18.5 micrograms). Intravenous injections of 0.001 Gm. of atropine produced decrease of blood iodides in all but 3 patients. Determination of blood iodides in 88 patients with various dermatoses (5 to 21 micrograms) showed no relation to their basal metabolic rates (—11 to +90 per cent). Study of the blood iodide content in 8 patients with dermatitis herpetiformis showed it to be slightly elevated in only 2 while the iodide content of the skin was greatly increased, to 552 and 304 micrograms per hundred cubic centimeters respectively (normal 70 to 90 micrograms). The authors conclude that there is no definite relation between blood iodine and dermatoses which are often accompanied by lability of the sympathetic nervous system. The intradermal iodine test (injection of 0.2 cc. of 0.8 per cent sodium iodide solution) in 80 patients with dermatoses showed 28 per cent positive reactions as compared with 31 per cent positive reactions in normal persons.

EXCRETION OF MELANOGEN IN BREAST MILK. H. GOTTRON and W. GERTLER, Arch. f. Dermat. u. Syph. **181**:91, 1940.

A woman aged 25 was seen in January 1938 with an enlarging, reddish nodule on the right side of the back. Thormählen's test for melanogen in the urine always gave positive reactions. Melanoma was diagnosed and roentgen therapy was used. In July 1938, during the seventh month of pregnancy, enlarged lymph nodes were present in the axilla. Thormählen's test of the urine showed a positive reaction. Severe headache and leg ache were attributed to metastases demonstrated by roentgenograms. After delivery, the breast milk gave a positive Thormählen reaction, as did the infant's urine at the age of 5 weeks. The reaction was negative while the child was fed artificially but again became positive while the child was on the breast.

CLIMATOPHYSIOLOGY AND CLIMATOPATHOLOGY OF THE SKIN: RELATION OF CLIMATE TO EPIDEMIOLOGY, ETIOLOGY AND BACTERIOLOGY OF THE PYODERMAS IN CENTRAL ANATOLIA. A. MARCHIONINI and S. TOR, Arch. f. Dermat. u. Syph. **181**:239, 1940.

The authors studied the influence of climatic factors on the epidemiology and pathogenesis of ubiquitous dermatoses. Patients with pyoderma constitute 36 to 37 per cent of the total clientele of the dermatologic clinic at Angora, Turkey. Other localities which combine tropical, semitropical and arctic climate also show extensive spread of pyodermas. The hygiene of the peasants of central Anatolia is excellent; so the increase cannot be attributed to lack of cleanliness. Bacterial studies showed the peasants' faces to be sterile.

Pyodermas are more frequent in the summer months. Young persons were involved more frequently than old. Crusted lesions predominated, then bullous and follicular pustules and finally furuncles and ecthyma. Differences in the meteorologically dissimilar years of 1938 and 1939 suggest that climatic influences, especially ultraviolet radiation and high temperature, play a role in the production of pyodermas. Experimental exposure of the skin to ultraviolet rays (erythema)

and elevation of the temperature produce an increase in sugar, calcium and catalase content but a decrease in acidity and diastase content. These effects tend to induce infection, as does loosening of the texture of the skin produced thereby. Sandstorms result in a high dust content of the air, especially for farmers in summer and autumn months. Sand flies are numerous during hot, dry weather; the cooler, more humid summer of 1939, with decreased numbers and shortened swarming time, was associated with a decreased incidence of pyoderma as contrasted to that of 1938. Scabies is most frequent during the winter, when pyodermas are less frequent. Vitamin A deficiency was not demonstrated in 5 patients with severe furunculosis. Staphylococci were found more frequently than streptococci.

PULMONARY ROENTGENOLOGIC OBSERVATIONS IN GRANULOMA FUNGOIDES. J. WERTH, Arch. f. Dermat. u. Syph. **181**:299, 1940.

Roentgenograms of 2 patients with granuloma fungoides were examined, and the study was repeated after an interval of about one year.

In both the hilar shadows were enlarged. Extending from these regions into the lungs were linear and spotty shadows. Reexamination after some months revealed accentuation of the signs in both instances. Since this picture suggests that seen in Boeck's sarcoid, inoculations of animals (guinea pigs and rabbits) with material from the tumors were made, with negative results. The author suggests that the causative agent of granuloma fungoides may be in the virus group.

RELIABILITY OF SEROLOGIC TESTS FOR SYPHILIS IN PREGNANCY. HANS KANDLER, Arch. f. Dermat. u. Syph. **181**:315, 1940.

Blood tests (the Wassermann test performed with several antigens, Kahn test and Meinicke clearing test) of 10,354 pregnant women in Dresden showed the following results:

Specificity was as great as in nonpregnant women. Two-tenths per cent nonspecific reactions were obtained with the Kahn test, 0.23 per cent with the Wassermann and 0.32 per cent with the Meinicke. Sensitivity of all three reactions is greater than in nonpregnant women. Syphilitic pregnant women showed 86 to 87 per cent positive and doubtful reactions by all the methods. With the Meinicke test there were 31.13 per cent doubtful reactions, with the Wassermann 12.41 per cent and with the Kahn 13.11 per cent.

Verification of syphilitic infection must be made for the pregnant woman as well as for the nonpregnant woman.

RETICULOSARCOMATOSIS. I. MAYER and S. WOLFRAM, Arch. f. Dermat. u. Syph. **181**:327, 1940.

A woman aged 36 had two small cutaneous tumors on the left arm and near the left breast. Nine months later a maculopapular exanthem appeared on the face and arms. Shortly afterward the macules and nodules increased to large partly ulcerated nodes covering the entire surface and to some extent the visible mucosae. The blood picture remained normal. She died seven months later of cachexia.

Autopsy showed general overgrowth of reticular cells of tumor-like character, especially in the skin and mucosae. The tumors were not sharply circumscribed but rather infiltrated the normal tissue. There was no primary tumor and no definite metastasis. The endothelial cells showed no proliferation with the exception of Kupffer cells. There were no monocytes in the infiltrate.

The condition corresponds to the differentiated form of reticulosarcoma (Oberling), polymorphous-celled forms of these tumors (Ahlström), mature retothelsarcoma of Roulet, polymorphous-celled retothelsarcoma of Oliveires and mixed cell retothelsarcoma (Rössle). Since it is a systematized disease of the cells of the reticulum, it is best designated as reticulosarcomatosis in the group of hemoblastomas.

TUBERCULIDS IN CHILDREN. P. W. SCHMIDT, Arch. f. Dermat. u. Syph. **181**:357, 1940.

In a cooperative study by dermatologists and pediatricians, clinical, immunologic and microscopic observations are presented of several types of tuberculids seen in 12 patients. The diagnoses were:

(1) and (2) lichen scrofulosorum, (3) circinate tuberculosis lichenoides, (4) eczematoid tuberculid following varicella, (5) lichenoid tuberculid, (6) papulonecrotic tuberculid, (7) papulopustular tuberculid, (8) miliary tuberculosis, (9) sarcoid (Boeck) and (10), (11) and (12) submiliary tuberculosis in children with tuberculous meningitis.

The authors believe that microscopic study aids in differentiation and in determining the prognosis.

BECKER, Chicago.

A CASE OF CHROMHIDROSIS ROSEA. I. YOSHIHIRO AND G. ARAKI, Jap. J. Dermat. & Urol. **47**:1 (Jan.) 1940.

A case of chromhidrosis rosea in a girl aged 19 is reported. Sweat stained the underclothing pinkish red. The only abnormality found on general examination was indicanuria. Daily oral administration of 3 Gm. of sulfur during one month resulted in the disappearance of chromhidrosis and indicanuria.

PELLAGRA IN CHOSEN (KOREA): II. CLINICAL AND STATISTICAL OBSERVATIONS ON PELLAGRA IN 1939. K. URABE, Jap. J. Dermat. & Urol. **47**:2 (Jan.) 1940.

In the first six months of 1939 the author observed 38 cases of pellagra in Chosen. The persons affected were mostly poor and between the ages of 20 and 35. April, May and June showed the greatest incidence of cases. The first cutaneous manifestation was the so-called *érythème pellagroïde* located on the back of the hands and feet, neck, chest, abdomen, genitals and face. Some patients showed the pellagrous mask and Casal's neck band. Most of them had gastrointestinal disturbance, and 8 showed the pellagrous tongue. In 10 cases there was associated an obstinate peripheral neuritis and in 8 a moderate Romberg sign, and 1 patient had psychosis. All the patients showed anemia, the moderately affected showing 70 per cent hemoglobin (Sahli) and those with the severe form less than 20 per cent. The blood coagulation time was increased. Pharmacologic investigation of the vegetative nervous system revealed abnormal tension. Most patients showed disturbance of the hepatic function and gastric achylia. The content of *l*-ascorbic acid in the urine was on the average diminished, the smallest figure being 0.98 mg. per hundred cubic centimeters.

RELATION OF HEPATIC DAMAGE TO CUTANEOUS DISEASE: II. NINE CASES OF ERYTHRODERMA EXFOLIATIVUM GENERALISATUM. M. IWAMA, Jap. J. Dermat. & Urol. **47**:14 (Jan.) 1940.

In 9 cases of erythroderma observed by the author disturbance of different visceral organs was present. There were hepatic and renal insufficiency and a gastrointestinal disturbance which manifested itself clinically and was proved by laboratory tests. In all the cases examination of the blood showed mild or severe eosinophilia and nuclear deviation of the leukocytes to the left. In most cases there gradually developed leukocytosis and lymphocytosis, but after improvement of the cutaneous disease the blood picture became normal. In 1 case there were anemia, leukopenia and eosinophilia, but gradually eosinopenia and lymphocytosis developed, after which the patient died in coma. In all cases except 2 hepatorenal insufficiency, pancreatic disturbance and abnormality of the gastric juice disappeared simultaneously with improvement of the cutaneous condition following injections of insulin and dextrose and administration of vitamin B.

STUDIES OF PELLAGRA IN CHOSEN (KOREA): III. AUTOPSY OBSERVATIONS IN PELLAGRA. K. URABE, Jap. J. Dermat. & Urol. **47**:27 (Aug.) 1940.

In 1939 the author observed 42 patients with pellagra, 1 of whom died. The essential observations revealed at necropsy were central hemorrhage and stasis atrophy of the liver and considerable deposition of hemosiderin in the dendritic cells of the liver. In the Virchow-Robin space of the cerebellar vessels there were yellow-brown pigment granules and thrombosis in a small vessel of the granular layer of the cerebellum.

CONJUNCTIVAL INFECTION OF LYMPHOGRANULOMA VENEREUM AS THE CAUSE OF PARINAUD'S DISEASE. T. HASHIMOTO, M. MIKUNI and Y. ISAKA, Jap. J. Dermat. & Urol. **47**:28 (Aug.) 1941.

The authors observed a case of Parinaud's disease due to lymphogranuloma venereum, which is the fourth case reported in the Japanese literature. The patient was a man aged 34 who three years previously had right inguinal adenitis which was treated surgically and was healed two months later. Six months preceding this report the patient injured the cornea of his right eye with a bamboo leaf, which produced considerable pain and also erythema, edema, visual disturbance and lacrimation. This ocular involvement was resistant to therapy. Examination revealed edema of the eyelids of the right eye, hyperemia, papillary vegetation and trachoma-like granulation of the conjunctival mucosa.

The cornea showed in the center a ringlike parenchymatous opacity with deep blood vessel formation and pannus with infiltration at the periphery of the cornea. There was moderate secretion of the eye. No micro-organisms were found. The Frei reaction was strongly positive. Frei antigen prepared from the secretion of the eye elicited a positive reaction in 5 patients with lymphogranuloma venereum and no reaction in 6 control cases. Mice given injections of this secretion had characteristic encephalitis, and an emulsion of their brains yielded an effective Frei antigen. Smears of the mouse brains revealed Miyagawa corpuscles. The patient was successfully treated with sulfanilamide. The author believes that involvement of the eye was probably due to a reinfection from the patient's wife.

TREATMENT OF ANGIOMA CAVERNOSUM WITH ROENTGEN RAYS AT CLOSE RANGE. K. SŌ, Jap. J. Dermat. & Urol. **47**:30 (Aug.) 1940.

The author reports successful treatment of cavernous angiomas of the face by means of roentgen radiation at close range, with 60 kilovolts, 40 milliamperes, filtration with 0.25 mm. of copper and 0.5 mm. of aluminum and 3 cm. focus-skin distance. The apparatus employed, which is manufactured in Japan, yields 66.6 r per minute. Two hundred roentgens is used at each exposure on three consecutive days. A second course of treatment is given after an interval of three weeks. The treatments may be repeated a number of times. The author states that the moderately large angioma cavernosum is made to disappear usually by 3,000 to 3,600 r of radiation at close range in the course of four months.

INFLUENCE OF VITAMINS ON INFECTION: II. INFLUENCE OF VITAMIN B_1 [THIAMIN] DEFICIENCY ON PYOGENIC INFECTION. K. TAKENOUTI, Jap. J. Dermat. & Urol. **47**:13 (Jan.) 1940.

Experiments with rats revealed that vitamin B_1 (thiamine) deficiency delays healing of wounds and increases considerably the mortality following infection.

INFLUENCE OF VITAMINS ON INFECTION: III. INFLUENCE OF VITAMIN B_2 [RIBOFLAVIN] DEFICIENCY ON PYOGENIC INFECTION. K. TAKENOUTI, Jap. J. Dermat. & Urol. **47**:35 (Feb.) 1940.

Sixty-five per cent of rats fed a diet deficient in vitamin B_2 (riboflavin) showed within thirteen to eighteen days alopecia of the eyelids and ocular involvement.

In seventeen to thirty-two days erythema and slight crusting appeared on the ears, extremities and tail. Occasionally the edge of the ear or the tip of the tail became necrotic and fell off. The influence of vitamin B_2 on bacterial infection proved to be slight.

INFLUENCE OF VITAMINS ON INFECTION: IV. INFLUENCE OF VITAMIN C [ASCORBIC ACID] DEFICIENCY ON PYOGENIC INFECTION. T. TAKENOUTI, Jap. J. Dermat. & Urol. **47**:36 (Jan.) 1940.

Deprivation of vitamin C (ascorbic acid) produced in guinea pigs loss of weight, locomotor disturbances and osseous changes. Following a slight infection, almost all the animals which had latent or complete vitamin C deficiency died. Thus vitamin C plays an important role in protection of the organism against pyogenic infection.

INFLUENCES OF VITAMINS ON INFECTION: V. INFLUENCE OF VITAMIN D DEFICIENCY ON PYOGENIC INFECTION AND RÉSUMÉ OF THE INVESTIGATIONS TO DATE. K. TAKENOUTI, Jap. J. Dermat. & Urol. **47**:53 (March) 1940.

Rats fed on a diet poor in vitamin D lost weight and had locomotor disturbances, spastic position of the toes, alopecia and, finally, kyphosis, scoliosis or the typical rachitic rosary. There was also disturbance of ossification in the knee joint. Wound healing was delayed, and mortality following infection was high. Thus vitamin D proved to be a protection against infection. The author found that the vitamins A, B, B_1, B_2, C and D all protect the organism against infection but that vitamin C is most effective in this respect. BLOOM, New York.

CUTIS GYRATA OF UNUSUAL LOCATION. S. RUDBERG, Acta pædiat. **27**:67, 1939.

The term cutis gyrata refers to thickening, redundancy and plication of the skin in such a manner as to impart to the region affected an aspect suggestive of the appearance of the cerebral cortex; the anomaly bears a number of names. It was first described by Robert, in 1848. Subsequent publications have brought the number of reported cases to about 250. Middle-aged men appear to be most commonly affected. Since the commonest location of the lesion is the scalp, where long hair is apt to conceal it, it is probable that the frequency of its occurrence in women has been somewhat underestimated. It is said to be rare in children. The histologic features are sometimes those of inflammation, sometimes those of a nevus and sometimes merely thickening of the subepidermal connective tissue. Its etiology and pathogenesis are obscure. It has been thought to bear some relation to endocrine disorder, particularly to acrodynia. Some authors regard it as a manifestation of diverse causes and others as a degenerative consequence of advancing age. The analogy between cutis gyrata in man and the redundancy of the skin of the skull which characterizes certain canine species has led some writers to talk of atavism. In favor of its developmental origin is the fact that associated somatic anomalies are not infrequently present. Truffi described three varieties: (1) a congenital nevus, (2) an inflammatory lesion and (3) a congenital defect of development involving a disproportion between the skull and its integument, often associated with other anomalies. Fischer's classification contains the same elements.

The author reports the case of a newborn child with cutis gyrata; the lesion involved the skin of the abdomen. A cutaneous scar suggestive of adhesion to the amnion was present on the right lower extremity, and the ears were deformed. Autopsy revealed anomalies of the urinary tract and defects of the abdominal musculature. Microscopically, the gyrate epidermis was somewhat acellular and showed a deficiency of elastic fibers. In this case the lesion is interpreted as an anomaly of development. The bibliography is elaborate.

McCUNE, New York. [AM. J. DIS. CHILD.]

Society Transactions

LOS ANGELES AND SAN FRANCISCO DERMATOLOGIC SOCIETIES

H. C. L. LINDSAY, M.D., *Chairman*

SAUL S. ROBINSON, M.D., *Secretary*

Joint Meeting, Los Angeles, Feb. 22, 1941

A Case for Diagnosis (Lupus Erythematosus? Leprosy?). Presented by DR. NELSON P. ANDERSON, Los Angeles.

G. C. S., a man aged 53, had a furuncle-like lesion on the flexor surface of the left forearm which developed in July 1940. It was painful and sensitive but did not "come to a head." Four or five days after the acute onset the lesion was incised by a physician, and ten days later an eruption appeared that was especially located on the scalp, knees and toes. The lesions were described as resembling "boils," but the overlying skin opened and discharged only serum. The patient at this time received several roentgen ray treatments. He noted that the tips of the fingers and toes were numb and presented the "pins and needles" sensation of going to sleep. A diminution of vision and a tingling sensation in the anterior half of the left side of the tongue were noted. The patient has gradually lost weight and strength. Muscular weakness has developed in the arms and legs. The examination shows atrophic, violaceous and erythematous round pea-sized lesions on the anterior aspects of the left and right forearms and the anterior surfaces of the knees. There are similar scattered lesions on the trunk. The Wassermann reaction of the blood and of the spinal fluid was negative.

Resistant Lupus Erythematosus Treated with Liver Extract. Presented by DR. CHRIS HALLORAN, Los Angeles.

A. F., a man aged 26, has had an eruption on the ears, face and scalp for eight years. Many medicaments, including gold sodium thiosulfate, have been employed in the therapy of his lesions. There has never been any complete remission in the eruption. In July 1940 the patient was given a course of liver extract in doses of 0.4 cc. of boiled liver extract twice weekly intramuscularly. The cutaneous lesions rapidly showed definite signs of improvement. The examination now reveals numerous areas of active and inactive discoid lupus erythematosus. There are many atrophic areas from former large lesions.

DISCUSSION

DR. N. N. EPSTEIN, San Francisco: These cases appear to be typical instances of lupus erythematosus. It seems to me that in the therapeutic approach to lupus erythematosus the safest method of treatment is the use of bismuth subsalicylate intramuscularly. A bismuth compound should be used first before one administers the gold salts or before any other method of treatment is used which might stir up the process.

DR. CHRIS HALLORAN, Los Angeles: My patient with lupus erythematosus was presented because of the interest in the problem of therapy. At first he was given a course of gold sodium thiosulfate, to which the lesions responded, but a point was reached after which further gold therapy failed to cause improvement,

even though the dose was increased to 100 mg. He then received a bismuth compound intramuscularly, with which medication he made further improvement, but then he also became treatment-fast to this drug. The patient again received gold therapy but experienced malaise and nausea after each treatment, and so gold therapy was again discontinued. We recently administered boiled liver extract (Lilly) 0.4 cc. intramuscularly twice weekly. With this medication the eruption almost entirely cleared. However, in the past three or four weeks the condition has again become stationary. I do not know in what manner liver extract would influence lupus erythematosus, but in this case there was definitely more improvement with liver than with either gold or bismuth.

Dr. N. P. Anderson, Los Angeles: I do not believe that my patient has a light-sensitive dermatosis. The lesions in the scalp today are those of cicatricial alopecia, with some activity. I do not believe that they belong in the category of lupus erythematosus. Dr. Hamilton Montgomery, of Rochester, Minn., has seen the histologic section from this case and has had the clinical history. He suggested that perhaps the condition might be a peculiar type of leprosy.

Dr. Samuel Ayres Jr., Los Angeles: In regard to the use of liver extract in lupus erythematosus, I should like to ask Dr. Halloran why he administered boiled liver extract instead of the unheated product. My only experience with liver extract in the treatment of lupus erythematosus was in a patient who apparently had all foci carefully checked and who had extensive treatment with gold and bismuth compounds without receiving any benefit. She now has had perhaps ten or twelve injections of unboiled liver extract in doses of 2 cc. at about four to five day intervals. Despite this the lesions continued to spread.

Granuloma Annulare. Presented by Dr. N. P. Anderson, Los Angeles.

R. A., a white woman, complains of an erythematosus annular eruption that first appeared four years ago on the right elbow. Involving the extensor surfaces of the elbows and the anterolateral surfaces of the upper part of the arms are typical lesions of granuloma annulare. The lesions are large and plaquelike with slightly infiltrated erythematous to purplish slightly elevated borders. Central clearing is present. Similar but smaller (dime-sized) lesions are present on the backs of the hands and fingers.

Sarcoidosis Cutis. Presented by Dr. Saul S. Robinson, Los Angeles.

M. M., a Jewish man aged 76, states that about four months ago bluish red ringlike lesions appeared on the flexor surfaces of the forearms. These lesions gradually enlarged, and one month ago similar areas appeared on the shoulders, upper part of the chest, neck, arms, trunk and face. Many discrete and confluent round elevated pinhead-sized to split pea–sized reddish brown papules and nodules cover the shoulders, chest and extensor surfaces of the arms and forearms. Some areas are in the form of plaques. Discrete dollar-sized nodular bluish red arciform lesions with central clearing are on the wrists. On physical examination the chest and abdomen were normal. Scrapings from the ear lobes were negative for lepra bacilli. The blood and urine were normal. Roentgenograms of the chest and phalangeal bones were normal. The reaction to an intradermal tuberculin test was negative with dilutions of 1 : 10,000, 1 : 100,000 and 1 : 1,000,000 of old tuberculin. The microscopic examination showed groups of epithelioid cells and occasional Langhans giant cells in the upper part of the cutis, compatible with the diagnosis of sarcoid of Boeck. Acid-fast stains of histologic sections for tubercle and lepra bacilli were negative.

DISCUSSION ON CASES OF DR. ANDERSON AND DR. ROBINSON

Dr. Donald H. Williams (by invitation), Vancouver, British Columbia, Canada: In the case of granuloma annulare the condition is one of the most extensive ones that I have seen. I do not believe that the problem is of diagnostic

significance. As regards the therapy in these cases, filtered roentgen rays administered to small lesions seem to give satisfactory results.

DR. HIRAM MILLER, San Francisco: I am unable to make a diagnosis of granuloma annulare from the present appearance of this patient's eruption. The size and color of the lesions and their location and configuration are more compatible with a diagnosis of sarcoid. I realize that there may be considerable clinical and pathologic similarity between these two conditions, and perhaps such a differentiation in this case is not important. In regard to the patient presented with the diagnosis of sarcoidosis, I wish to state that I have a patient under my care with a similar eruption which I have classified as a lichenoid tuberculid. She had an associated iritis, which was attributed to tuberculosis by her ophthalmologist. The only treatment which was of value in her case was rest in bed, vitamin therapy and tuberculin. She gained 25 pounds (11 Kg.) in weight, and her eruption and iritis cleared. The eruption recurred to a slight extent during the past winter months when the injections of tuberculin were discontinued.

Palmar Lichen Planus. Presented by DR. KENDAL FROST, Los Angeles.

W. F., a laborer aged 45, states that an eruption first appeared on his left hand six years ago and gradually spread to involve the entire hand. Later a few patches developed on the right palm. Except for the appearance, the patient's only complaint is the horny thickness of the palm. The lesions were first examined on June 17, 1940. There is less palmar horny thickening now than at that time. On the right palm are a few thick nummular areas with considerable horny scales. The left hand is entirely covered by bluish red infiltrated dry and scaly lesions chiefly limited on the wrist by a configurate border. Over most of the hand the surface is smooth and shiny. On the dorsal surface of the thenar web are individual angular patches. When first seen, the palm was covered with heavy dry keratotic scales. These have considerably lessened under treatment, so that at present only the underlying changes in color are still present. When the patient was first seen there were a few white papules on the inner surface of the lower lip. Otherwise there are no other lesions of the skin. The microscopic examination showed that the stratum corneum was moderately but distinctly thickened. Here and there were localized areas which were thickened and dipped down slightly into the depressions in the granular layer. In these thickened areas was seen an occasional body, which may have been a nucleus. The stratum granulosum was heavily pigmented. In the stratum malpighii were areas showing vacuolation. The basal cell layer was considerably broken in spots. In the papillary portion of the corium were heavy infiltrations of round cells and some fibroblastic proliferations.

The treatment has consisted of the administration of red mercuric iodide N. F. by mouth, mercury salicylarsenate intramuscularly and mercury bichloride intramuscularly. Roentgen ray exposures (50 r) were given to both sides of the hand approximately once a week for eighteen weeks. There has been very little change in the lesions. There is less of the cornification of the palm than at the beginning of treatment, but the lesion is much the same as in June 1940.

A Case for Diagnosis (Erythema ab Igne? Lichen Planus?). Presented by DR. C. RUSSELL ANDERSON, Los Angeles.

J. L., a white man aged 74, believes that his eruption developed as a result of his habit of sitting in front of a gas heater with his legs exposed. The duration of the lesions is six to seven months. Over the inner aspect of the left leg at the level of the knee and fading above and below is a reticulated area. The area at the knee is infiltrated and hyperkeratotic. There is some evidence of livedo reticularis on the inner aspect of the right leg. The microscopic examination showed moderate hyperkeratosis. The epidermis was atrophic. There were considerable edema and granular degeneration of the upper part of the cutis and a moderate perivascular infiltrate in the midcutis.

Lichen Planus Involving the Palms. Presented by Dr. A. F. Hall, Santa Monica, Calif.

M. G., a man aged 71, had been receiving treatment since July 1940 for an infectious eczematoid dermatitis of the right leg, left elbow and ears, which responded readily to local therapy. In January 1941 a few violaceous papules were noted on the flexor surfaces of the forearms and on the abdomen. The clinical diagnosis was lichen planus. Hard, flesh-colored papules somewhat resembling arsenical keratoses were later noted on the palms, and lesions suggestive of hypertrophic lichen planus appeared on the ankles. The patient is a heavy drinker of wine. Aside from the possible exposure to arsenic from fruit sprays (the patient makes his own wine from grapes), there is no known history of exposure to arsenic. On the forearms and abdomen are many flat-topped, angular violaceous papules typical of lichen planus. The lesions on the palms resemble arsenical keratoses more than a classic lichen planus. On the ankles are large nodular plaques surrounded by several smaller violaceous nodules typical of hypertrophic lichen planus. The urinary arsenic is 0.035 mg. per liter (normal). The Wassermann and Kahn reactions of the blood were negative.

DISCUSSION ON CASES OF DR. ANDERSON AND DR. HALL

Dr. H. J. Templeton, Oakland, Calif.: I thought that the diagnosis of erythema ab igne was proved by the way the elderly patient toasted his shins. He said that the gas heater was over to his right and that he always crossed his left leg over his right knee so that the involved area was exposed to the heat.

Dr. A. F. Hall, Santa Monica, Calif.: I should like to rise in defense of the diagnosis of lichen planus for my patient's condition. The only reason the case was presented was because of the peculiar keratoses in the palms, which suggest arsenical keratoses. The urine was examined for arsenic, and the results were interpreted as being within normal limits, while the microscopic picture of the lesions on the palms and arms was reported as being typical of lichen planus.

Dr. Kendal Frost, Los Angeles: The lesions in my patient with palmar lichen planus were less prominent today than they have been recently. The microscopic picture is so characterized that I thought it unnecessary to present it here. The case is presented primarily for demonstration of the unusual localization of lichen planus and for therapeutic suggestions. I have exhausted most of the ordinary means of treatment, with only about 50 per cent improvement.

The diagnosis for the patient with a possible erythema ab igne has aroused some discussion at the monthly conferences at the Los Angeles General Hospital. There is no doubt that the man has erythema ab igne. There are in places flat angular papules in the reticulum of pigmentation which have been very suggestive of lichen planus. The histologic picture is also somewhat in accord with this diagnosis, and I agree that this patient has lichen planus which is localized in this unusual manner owing to a circulatory disturbance.

Dr. N. P. Anderson, Los Angeles: I examined the patient with the diagnosis of palmar lichen planus from a clinical standpoint. I suggest a diagnosis of a Trichophyton purpureum infection of the palm because the other palm seems to be without any involvement. The fact that the mucous membranes are involved in this infection is entirely compatible with that diagnosis. This observation is true in spite of the fact that the condition partially responded to roentgen rays, with the addition of arsenic and mercury therapy.

Lupus Vulgaris. Presented by Dr. Ben A. Newman, Los Angeles.

M. N., a white woman aged 30, states that her father died of pulmonary tuberculosis two years ago. During childhood her ears were frostbitten several times. At the age of 13 a lesion appeared on the right external ear. The lesion slowly increased in size until four years ago, when it occupied most of the helix. A cautery excision of the lesion was done. The patient was then free of the

growth for three years until a recurrence began one year ago. The eruption is composed of soft brownish yellow papules and nodules dispersed over the formerly excised margin of the ear. On diascopic pressure the typical apple jelly nodular appearance is visible. The patient is in excellent health. A physical examination and a roentgenogram of the chest were entirely normal. Intradermal tuberculin tests elicited positive reactions with a dilution of 1:500,000 of old tuberculin. The microscopic examination showed a typical collection of epithelioid cells and lymphocytes with central giant cells.

Livedo Reticularis. Papulonecrotic Tuberculids. Presented by DR. BEN A. NEWMAN, Los Angeles.

L. C., a white woman aged 20, at the age of 11 years attended a pediatric clinic because of being underweight. At that time she was found to have a positive reaction to a Mantoux test and roentgenograms of the chest showed a thickened hilus with fibrocalcific deposits in the tracheobronchial lymph glands. At no time thereafter was there any evidence of active tuberculosis. One year ago the patient first noticed a bluish mottling of the skin of the lower extremities. She has always had cold extremities. The examination at that time showed bluish reticulated marbling extending from the ankles to the middle part of the thighs. During July and August 1940 the skin was clear. The mottling returned this past fall and also involved the elbow region. One month ago crusted lesions appeared about the ankles. The patient now presents the typical bluish vascular network of livedo reticularis involving both lower extremities and the skin just above and below the elbows. Above each malleolus is a slightly tender crusted papule about the size of a small pea. The patient is in good health and of normal weight. On physical examination she was normal. A roentgenogram of the chest was normal. The reaction to an intradermal tuberculin test was positive with a dilution of 1:1,000 old tuberculin. The examination of the blood during the past two years has shown a persistent leukopenia, with a leukocyte count varying from 3,000 to 4,000 per cubic millimeter. The patient has had about fifteen treatments of mecholyl chloride (acetylbetamethylcholine hydrochloride) iontophoresis, without benefit. Treatment with prostigmine bromide did not change the vascular pattern.

DISCUSSION ON CASES OF DR. NEWMAN

DR. FRANCES TORREY, San Francisco: I agree with the diagnosis of lupus vulgaris. I understand that the lesion on the lobe of the ear is an extension after excision of the upper portion of the rim and that the cutaneous lesion is of long duration. The patient has systemic tuberculosis also with a history of childhood contact with her father, who had pulmonary tuberculosis. Besnier has pointed out that patients with pulmonary tuberculosis do not acquire lupus, whereas patients with lupus frequently have pulmonary tuberculosis. There are two problems to consider in this case. The first is the control of the systemic tuberculosis and the second the cutaneous lesion. If roentgen ray therapy has not been used, I suggest that it be considered for the small active area of tuberculosis on the ear.

The patient with livedo reticularis and papulonecrotic tuberculids is also one who has some systemic disease. Although the patient has no clinical evidence of pulmonary tuberculosis she has a symmetric distribution of the cutaneous lesions on the legs suggestive of a toxic manifestation. The vasomotor disturbance evidenced by the livedo reticularis suggests the vascular changes accompanying erythema induratum in girls of this type. This vasomotor instability and vascular stasis may be the explanation of the ulcerative lesions in these areas.

DR. A. F. HALL, Santa Monica, Calif.: In the record of the case of livedo reticularis and papulonecrotic tuberculid, it was stated that the patient was sensitive to tuberculin, the reaction to an intradermal test being positive with a 1:1,000 dilution. I should like to ask if that was misprinted. Was the patient sensitive to a greater dilution? I think that a positive reaction to a 1:1,000 dilution of

tuberculin would not have much significance from a diagnostic standpoint. In the case of lupus vulgaris there was a positive reaction to a 1:500,000 dilution of tuberculin. I wonder if any diagnostic significance could be placed on any positive reaction to a 1:1,000 dilution of old tuberculin in an adult.

Dr. Ben A. Newman, Los Angeles: This patient was sensitive only to dilutions of 1:1,000. This patient from the age of 15 to 21 years came to the clinic because of undernourishment. At that time she was found to have an infiltration at the base of the lungs. The physician who examined her at that time said that she had a latent pulmonary tuberculosis. I think that it is agreed that a positive tuberculin reaction in a child indicates a tuberculous infection.

A Case for Diagnosis (Linear Scleroderma?). Presented by Dr. N. P. Anderson, Los Angeles.

S. S., a girl aged 9 years, has a lesion involving the lower lip of nine months' duration, which occurred after a fall that bruised the lip. Following this trauma a small white spot appeared, which has increased in size and extended down on the mucous membrane on the inside of the lower lip. There is a small flat pea-sized white atrophic scarlike area involving the central portion of the vermilion border of the lower lip. Just to the left of the midline there appears a linear scleroderma-like thickening that extends onto the mucous membrane of the lower lip and downward inside of the mouth.

Dermatomyositis with Extensive Subcutaneous Calcification. Presented by Dr. N. P. Anderson, Los Angeles.

J. A., a girl aged 17, states that an eruption began about two and one-half years ago in the axillas. After the axillary involvement the skin all over the body became firm and hard and lesions developed on the hands, fingers and forearms. Examination disclosed atrophy of the shoulder girdle, heliotrope discoloration about the eyelids with edema, flexor deformity of the knee joints and scleroderma-like involvement of all the fingers, with redness of the ends of the fingers. Atrophic whitish areas are on the dorsa of the hands and fingers and on the extensor surfaces of the elbows. Roentgenograms of the thighs showed a deposit of calcium in the subcutaneous tissues.

Generalized Morphea. Presented by Dr. Samuel Ayres Jr., Los Angeles.

E. L., a woman aged 64, has an eruption that first appeared about nine months ago on the arms and about the waist. The lesions were purple areas which the patient stated would fade to a faint pink during the night. Areas of hardness and induration began on the chest about five or six months ago and on the arms about three months ago. There is no history of internal medication prior to the onset of the condition. Her teeth were all extracted about twelve years ago. The eruption now appears in extensive areas over the trunk, arms, legs and thighs, consisting of large plaques and bands of violet pink. Some of the lesions show central areas of waxlike shiny sclerosis. The hands and feet are free of involvement. The patient has received eight injections of gold and sodium thiosulfate and has been receiving 2 grains (0.13 Gm.) of thyroid daily. There has been some improvement.

DISCUSSION ON CASES OF DR. ANDERSON AND DR. AYRES

Dr. Hiram Miller, San Francisco: In my opinion the patient presented with dermatomyositis has a classic example of this disease. The disease may be seen at any age, but in most of the cases it occurs in young women. I am particularly interested in this disease from the therapeutic standpoint. In the final analysis there is little that can be done. Supportive measures in the form of rest,

good food and vitamin therapy are indicated. Physical therapy to prevent muscular atrophy and contracture is often necessary. Sulfanilamide has not been found to be of value in late stages, but it may be useful in early stages of the disease.

Dr. Herman Allington, Oakland, Calif.: I agree with the diagnosis in the case presented as one of linear scleroderma.

In the patient with dermatomyositis with extensive subcutaneous calcification I think that the clinical picture at this time could as easily be interpreted as a late stage of generalized scleroderma with sclerodactylia.

Dr. Donald H. Williams (by invitation), Vancouver, British Columbia, Canada: The girl with linear scleroderma has an exceedingly interesting condition. Two years ago I saw a girl 11 years of age with an identical slightly indurated fibrotic plaque on the mucous membrane of the lower lip, extending into the mouth. I was very much surprised that the histologic picture was taken for lichen sclerosus, as that is one condition with a characteristic histologic picture. I suggest the diagnosis of lichen planus in this case.

Dr. Samuel Ayres Jr., Los Angeles: In regard to Dr. Miller's remarks, I saw in consultation a young man who had a condition similar to the one presented in this case. The patient finally recovered after the use of an autogenous vaccine obtained from nasal secretions, as well as aminoacetic acid, gelatin and mixed vitamins.

Dr. N. P. Anderson, Los Angeles: I should like to exhibit a roentgenogram showing the tremendous calcification of tissues in this girl's thighs. I did not leave this roentgenogram with the patient, as I thought it was better that she did not see it.

Dr. C. Russell Anderson, Los Angeles: I disagree with the diagnosis in the case presented as one of generalized morphea. The patient has marked involvement of the hands and feet. The hands are bluish, and the patient states that when they become cold they are either bluish or white. There is an involvement of the connective tissues and also of the vascular system. I think that this case should be diagnosed as one of diffuse scleroderma. As regards the prognosis in these cases, seven or eight years ago I examined about 300 records of patients who had scleroderma with calcification. About 25 per cent of the patients eventually became almost clinically well. Involvement of the finger tips, calcification and ulceration would eventually clear up after a period.

Hereditary Hemorrhagic Telangiectasia. Presented by Dr. Chris Halloran, Los Angeles.

M. B., a white woman aged 54, has a history of attacks of bleeding from hemangiomas in the nose since the age of 15. The bleeding at times has been severe enough to necessitate hospitalization and blood transfusions. The examination shows hemangiomas on the tongue, buccal mucosa and nasal passages. Examination of the blood, including determination of platelets, bleeding time and clotting time, showed normal results except for 60 per cent hemoglobin. The fragility of the erythrocytes was within normal limits. There was no evidence of a blood dyscrasia.

Angioma Serpiginosum. Presented by Dr. Saul S. Robinson, Los Angeles.

M. G., a white woman aged 55, states that in August 1940 three red spots first appeared on the anterior region of the left ankle. The patient thought that these spots were insect bites. More lesions then appeared within twenty-four hours on the legs, ankles, thighs and trunk up to the level of the breasts. No subjective symptoms were noticed at first, but there is now a slight pruritus. There is no history of drug ingestion. On the legs, thighs and trunk are macular scaling areas composed in places of telangiectatic puncta. Some of the puncta have an annular

arrangement. There is a suggestion of atrophy in spots. The Wassermann and Kahn reactions of the blood were negative. The blood and urine were normal. The histologic examination showed atrophy of the epithelium with zones of degeneration in some of the papillae. Occasional zones of mononuclear exudate were present in the corium. There was no evidence of new blood vessel formation. Intraepithelial edema of a circumscribed type in the papillary layer was intense. The histologic picture was consistent with the diagnosis of early angioma serpiginosum.

DISCUSSION ON CASES OF DR. HALLORAN AND DR. ROBINSON

DR. HOWARD MORROW, San Francisco: I have been wondering since examining the patient presented by Dr. Halloran whether there would be any results from treatment with snake venom. She states that she bleeds frequently from the nose, tongue and pharynx.

DR. H. J. TEMPLETON, Oakland, Calif.: In any case of angioma serpiginosum the alternative diagnoses of Schamberg's disease, purpura annularis telangiectodes and Gougerot's chronic purpuric lichenoid dermatitis have to be considered. I had the pleasure of assisting Dr. Schamberg, and I think he should have called this case one of progressive pigmentary dermatosis. The lesions began on the legs with small cayenne pepper dots which spread into patches and then upward over the legs. I do not know whether the histologic sections were stained with prussian blue to see if hemosiderin was present, but I feel that morphologically this condition is an example of Schamberg's disease.

DR. BEN A. NEWMAN, Los Angeles: In view of the remark of one of the previous speakers that nothing can be done for telangiectasia, I wish to call attention to some possibilities of further investigation in this case. Recently I have been interested in the mechanism of production of the diffuse telangiectases that one not uncommonly encounters during pregnancy. I am referring to that type of telangiectasia which begins during the early months of pregnancy, extends over the body until the patient reaches term and disappears within two to three months post partum. There are two physiologic factors to account for this telangiectasia; one is an increased blood volume during pregnancy and the second is an increased progesterone level in the blood stream. Progesterone is known to relax smooth muscle and dilate blood vessels. Hence, the combination of this vascular dilatation and the increased blood volume may be the cause of the telangiectasia. The patient presented here stated that her menopause began two years ago, at the age of 38, concomitant with the appearance of the telangiectasia. In view of this history it is not at all unlikely that her menopause may be due to an increased progesterone level. I suggest that determinations be made of the progesterone excretion and the patient's blood volume. If abnormalities are found, therapeutic measures would then be possible for this disfigurement.

Tuberculosis Verrucosa Cutis. Presented by DR. CHRIS HALLORAN, Los Angeles.

B. S., a Mexican youth aged 16, was originally seen in the dermatologic clinic in 1935 because of a lesion the size of a 25 cent piece on the back of the left hand. The area has been removed twice by cauterization, and he has been treated with solid carbon dioxide, injections of tuberculin and immobilization of the hand. During the last two months he has been receiving weekly injections of starch directly into the nodule, with moderate improvement. The examination shows a verrucous lesion occupying the central portion of the dorsum of the left hand and extending down over the dorsa of the fingers. There are no systemic signs of tuberculosis. The microscopic examination showed a granuloma with irregular pseudoneoplastic acanthosis.

Tuberculosis Verrucosa Cutis. Presented by Dr. Irving Bancroft, Los Angeles.

A. C., a woman aged 53, had bilateral active pulmonary tuberculosis in 1936. About three years ago the eruption on her hand began as a small verrucous erythematous lesion which has steadily increased in size. The patient states that the lesion followed an injury at this site with a wood splinter. Involving the opposing surfaces of the left thumb and index finger are two fungating, erythematous, verrucous lesions. The histologic picture was compatible with cutaneous verrucous tuberculosis.

DISCUSSION OF CASES OF TUBERCULOSIS VERRUCOSA CUTIS

Dr. Arne Ingels, San Francisco: I agree fully with the diagnosis as presented. I felt that the tuberculosis verrucosa cutis in the Mexican boy was unusually hypertrophic in type, but then I also noticed that the condition was of long standing. I feel that the interest in these cases centers in the method of inoculation.

Pyoderma Gangraenosum with Ulcerative Colitis. Presented by Dr. L. F. X. Wilhelm, Los Angeles.

L. S., a white woman aged 19, has a history of an acute onset of diarrhea about two and one-half years ago. About two months ago a "boil" developed on the right side of the lower jaw that healed readily, but since then similar lesions have appeared behind the right ear, on the left hand and on both extremities. The lesions on the extremities and right hand have became progressively worse. On the back of the legs are two large patches of ulceration which originally were extremely necrotic and surrounded by devitalized areas of otherwise normal epidermis. There is a similar smaller patch on the right jaw and on the left hand. The patient is extremely cachectic and still has numerous attacks of diarrhea. Aerobic and anaerobic cultures of cutaneous lesions revealed only Staphylococcus albus. The examination of the stools for amebas was negative. The examination of the blood showed a severe secondary anemia. The values for free and combined gastric acidity were diminished. The lesions show 70 per cent improvement after treatment with sulfanilamide and azosulfamide (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′-disulfonate).

DISCUSSION

Dr. Herbert Lawrence (by invitation), Los Angeles: This patient is presented to show the progress since the presentation of one year ago at this meeting, since which time complete medical studies have been performed. A year ago the impression was that the condition was pyoderma gangraenosum with a concurrent amyloidosis of the spleen. At that time the spleen was down to the iliac crest and the liver was palpable beneath the costal margin. Members of the medical department did not feel that amyloidosis was responsible for the systemic picture that the patient presented, and the reaction to a congo red test, which was performed for the purpose of checking the diagnosis of amyloidosis, was found to be within normal limits. It was also felt that the tendency of the patient to recover and the normal renal studies were not in favor of this diagnosis. It was the opinion that the progressive development throughout the last six years of a massive spleen stood out as the most striking clinical observation, and the causes of splenomegaly were considered in the differential diagnosis. Chronic aleukemic splenomyelogenous leukemia was considered as one of the possible diagnoses. The persistent low grade fever, large spleen, petechiae and blood picture are consistent with this diagnosis. Another condition that was considered was a chronic mycotic generalized infection. However, tissue studies, as well as mycologic and bacteriologic examinations of the blood and bone marrow, did not reveal the etiologic agent. Leishmaniasis was considered because of the reversal in the albumin-globulin ratio, the hyperproteinemia and the presence of a generalized

systemic low grade infection. However, here again thorough studies for the etiologic agent (Leishmaniae) gave negative results. A third possibility considered in the diagnosis was splenic tuberculosis. However, it was felt that this last diagnosis could not be proved without a biopsy of the spleen. Two splenic punctures were performed on successive dates, and bacteriologic and mycologic studies revealed only the questionable presence of clumps of long, beaded bacilli which were indentified as belonging to the Actinomyces group. The bacteriologists were not certain that this was definite, but they presented the possibility of the diagnosis of splenic mycosis with which the clinical picture would be consistent. Some splenic pulp was recovered from the second splenic puncture and was considered normal. Further pathologic examination of the spleen is desired, and it is intended that a splenic biopsy will be performed in the near future. The diagnosis most in favor at present is mycosis of the spleen, probably due to an actinobacillus.

A Case for Diagnosis (Leprosy? Sarcoidosis? Fixed Drug Eruption?). Presented by DR. KENDAL FROST, Los Angeles.

M. H., a Mexican woman aged 58, entered the clinic with the lesions as presented of two months' duration. There is a history of taking many laxatives and other home remedies. The eruption appeared to be a fixed drug eruption, but there has been no change in the appearance of the lesions in spite of abstinence from all drugs. There is a dollar-sized indurated patch over the right eyebrow. A large, sleevelike lesion involves most of the midportion of the left arm and shows involution in the center and activity peripherally, where there is a raised, indurated border. There is a similar but much smaller lesion on the dorsum of the right ankle. There is no evidence of any systemic disease except that a roentgenogram of the chest shows a slight thickening of the apical bronchial and vascular detail, which appears insufficient to indentify tuberculosis at this time. There is a small amount of infiltration along the thickened basal trunk shadows consistent with early basal pneumonitis. The Wassermann reaction of the blood was negative. The reaction to a coccidioidin test was negative. Nasal scrapings, as well as blood smears from the ear lobe, were negative for acid-fast bacilli. The histologic examination showed a granulomatous lesion with tuberculoid structure. No acid-fast organisms were seen in the histologic sections.

DISCUSSION

DR. HIRAM MILLER, San Francisco: It is my opinion that this patient's eruption is a granuloma. I do not know whether it is leprosy or sarcoid. An increase in the pain reaction to pinprick is against a diagnosis of leprosy. The lepra bacilli should be found in histologic sections if the eruption is due to leprosy.

Squamous Cell Epithelioma of the Lower Lip. Tertiary Syphilis. Presented by DR. THOMAS NISBET, Los Angeles.

L. E., a man aged 37, one year ago presented a gumma involving the skin surrounding the right side of the left leg, which disappeared after four injections of neoarsphenamine. Treatment was then discontinued. Three months ago a small crusted lesion appeared on the left side of the lower lip, which rapidly spread and increased in size. During the past six weeks the patient has received four injections of neoarsphenamine and two of bismuth subsalicylate, under which therapy there has been no alteration in the lesion. During the past two weeks since the discontinuance of therapy the lesion has doubled in size. The lesion is about the size of a small plum, occupying the whole of the lower lip. Below the vermilion border is a dull red, inflammatory, nodular mass with multiple sinuses discharging a seropurulent exudate. The entire mucous membrane of the lower lip is distended with firm infiltrated nodules. The Wassermann reaction of the blood was positive. The histologic examination showed whorls and strands

of dyskeratotic epidermis penetrating and practically obliterating the corium. Keratinization was prominent. The pathologic diagnosis was squamous cell epitheloma, grade II.

DISCUSSION

DR. H. J. TEMPLETON, Oakland, Calif.: This case reminds me of a remark that one of the British syphilologists made, that lingual carcinoma is born on the bed prepared by syphilis. Although the location in this case is not lingual, I think that the epithelioma of the lip may well have been born on the bed of the syphilis which the patient had. In treating any epithelioma of the skin or mucous membrane, I believe that destructive measures always take precedence over radiation provided that the lesion is accessible. By destructive measures I mean either excision by electrosurgery or electrocoagulation. I treat all epitheliomas of the lip in my office by using either block local anesthesia or, if the lesion is extensive, double mandibular nerve blocking.

DR. FRANKLIN BALL, Hollywood, Calif.: I recall a case in which the tumor was probably not as large as in the case presented today, but it also was an epithelioma involving the entire lower lip. This patient received approximately 8,000 r of roentgen rays to the lesion. The effect of this dose was practically destructive to the entire affected area. In spite of this tremendous dose of roentgen rays the lesion was only held in check for about six months. It then metastasized to the lymph nodes in the surrounding areas. I believe that this is evidence that roentgen ray therapy, even in large doses, is probably not the best form of therapy and that other methods, such as electrosurgical destruction thoroughly done, are probably better methods of handling such cases. The plea of those who favor roentgen ray therapy because the end result may be less disfiguring to the patient should not be regarded as highly as it has been. The use of electrosurgery can always be followed by plastic repair.

DR. IRVING BANCROFT, Los Angeles: Statistics show that 85 per cent of patients suffering from carcinoma of the tongue have a positive Wassermann reaction. I have encountered in the last few years numerous instances in which there was a positive Wassermann reaction of the blood, and it was immediately assumed that the lesion on the tongue was due to syphilis, when it was really cancer.

DR. H. P. JACOBSEN, Los Angeles: It has been my good fortune to observe a great many cases of epithelioma of the lower lip, and I want to echo the sentiments expressed here as to the relationship of this type of lesion to syphilis. I am somewhat prejudiced, but I agree entirely with what Dr. Templeton has said. I do not agree that it is wise to treat these conditions by means of radiation therapy.

DR. N. N. EPSTEIN, San Francisco. The problem of carcinoma of the lip is one which deserves thorough consideration. I do not agree with Dr. Templeton or with Dr. Jacobsen. Epithelioma of the lip may or may not be a dermatologic problem. There are certain small epitheliomas of the lip which the dermatologist can destroy well. There are certain larger lesions which surgeons can treat better. Finally, roentgen ray therapy has a definite place in the treatment of cancer of the lip. Large lesions which result in too much deformity if destroyed or excised may do better with roentgen ray therapy. It seems to me that epithelioma of the lip concerns all three specialties, and the employment of each in its proper place will give the patient a better chance of cure. In the case under discussion, the lesion of the lip is large, and there is obvious metastasis to the neck. I think that roentgen ray therapy of the local lesion with dissection of the neck is the proper therapeutic approach in this case.

Dystrophy of the Nails Due to Mercury Poisoning. Presented by DR. CHRIS HALLORAN, Los Angeles.

W. L., a man aged 57, has worked at a mercury furnace for a long time. In 1938, after an attack of pyorrhea, his teeth became loosened and fell out. In October 1940 the nails started to shed. The nails of both hands and feet, beginning

about their midportion, are exfoliating. There is no evidence of a blood dyscrasia. The arsenic content of the urine was normal. Roentgenograms of the bones of the ankles and knees showed no pathologic changes. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. N. P. ANDERSON, Los Angeles: This patient presents peculiar changes in the nails which he ascribes to his work as an operator of a mercury furnace. If Dr. Halloran believes that these changes are due to the mercury, I wish he would tell me just what the mechanism is before I discuss this case. This man handles mercury, arsenic and antimony. This condition of onychomadesis has never been described as due to the action of mercury. Certainly, if it were due to the ingestion of mercury or its external use, cases of this kind should have been described previously. It is true that antimony sometimes produces changes in the nails. The same facts hold true for arsenic. Although this patient has a negative Wassermann reaction of the blood, he does have pupils that are irregular and unequal. He has no other signs of involvement of the central nervous system. I believe that before one can state that the disorder of the nails presented by this patient is due to any one of the chemicals which he is handling, a spinal puncture should be done to rule out syphilitic involvement of the central nervous system. The same condition is present to a lesser degree on both great toes and on both second toes. Therefore, if the condition is caused by chemicals it must be due to a systemic action and not to a local effect. In most of the cases of this type of involvement of the nails that have been described in the literature (Strauss, M. J.: Onycholysis and Onychomadesis: Report of a Case of Each, with a Review of the Literature, ARCH. DERMAT. & SYPH. **26**:644 [Oct.] 1932) the condition is due to either diabetes or tabes dorsalis.

DR. CHRIS HALLORAN, Los Angeles: This case was presented because of a history of mercury poisoning with associated loosening and loss of teeth associated with subsequent development of dystrophy of the nails. It would be impossible to be certain that the dystrophy of nails was produced by mercury poisoning. However, in this case the history together with the observation certainly strongly suggest that this is what has taken place.

DR. MERLIN MAYNARD, San Jose, Calif.: I believe that the condition in this case should be classified not as a contact injury but as a general intoxication, from whatever cause one wishes to choose. Mercury, antimony and arsenic all produce this type of damage to the nails. The growth of the nails has become static as a result of the poisoning, and with recovery the new nails are replacing exfoliated ones. This patient would absorb a large amount of the volatile metals, and the intoxication would be through this means rather than by direct contact.

DR. N. N. EPSTEIN, San Francisco: I should like to report an instance of desquamation of the finger nails which followed the use of mercurochrome intravenously when it was introduced some years ago. At that time large amounts of this drug were given to patients with gonorrhea. One of these patients had desquamation of his finger nails and loss of his teeth and hair.

A Case for Diagnosis (Chronic Erysipelas?). Presented by DR. CHRIS HALLORAN, Los Angeles.

R. H. T., a man aged 34, states that his cheeks and eyelids first began to swell three years ago. The swelling has gradually become worse, although periods of remission occurred up to two years ago. There are edema, redness and induration in the periorbital and temporal regions. The mycologic examinations suggest that a torula infection is the etiologic agent.

DISCUSSION

DR. C. O. WOOD (by invitation), Beverly Hills, Calif.: A physician at the Mayo Clinic was getting good results with injections of hot water into such

lesions. I observed 2 of these cases, in which the improvement was about 90 per cent.

DR. WALTER SCHWARTZ (by invitation), Pasadena, Calif.: When this patient was seen last month or the month before, the edema was limited to his eyelids. The diagnosis was uncertain at that time. The edema of the eyelids is the prominent observation today. Instead of the cutaneous condition being a local process, it is undoubtedly systemic. I wonder if the presenter has found anything that might explain this edema as due to a vascular cause. I believe that the edema and the puffiness of the eyelids are on the same etiologic basis as generalized edema.

Hidradenitis Suppurativa. Presented by DR. H. SUTHERLAND CAMPBELL, Los Angeles.

M. S., a girl aged 20, about three years ago had multiple purulent draining abscesses and sinuses in the axillas and groins. She was first seen in the clinic in July 1940, with the diagnosis as presented. She was hospitalized and treated with sulfanilamide and sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine), with moderate improvement in the lesions. She has received various types of local as well as supportive therapy. The present hospitalization was begun in October 1940, for the purpose of administering sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole). The administration of this drug succeeded in considerably diminishing the discharge. At present the patient is receiving roentgen ray therapy.

DISCUSSION

DR. SAMUEL AYRES JR., Los Angeles: I have not had the privilege of following this case, but my impression is that the condition is healing. I noticed that some adhesions were forming which would lead to restricted motion if they are not separated.

DR. CHRIS HALLORAN, Los Angeles: For the past two or three years I have been using sulfanilamide locally in the form of a 10 per cent paste or a 10 per cent powder in the treatment of chronic ulcers, such as varicose ulcers of long standing, with satisfactory results. In a case of pyoderma gangraenosum sulfanilamide and its derivatives were not tolerated by mouth but there was decided improvement after the application of a 20 per cent sulfanilamide ointment. The patient apparently had not absorbed the drug sufficiently to produce any toxic reactions.

DR. FRANKLIN BALL, Hollywood, Calif.: I agree with the diagnosis of the presenter in this case, but since he has requested suggestions on therapy I should like to comment that I think that this case represents the usual therapeutic management through which most sufferers of this disease are directed. The results of treatment are generally discouraging, and I think that this patient will eventually require surgical intervention and thorough excision of the affected areas followed by plastic surgery. Of all the suppurative lesions that one might see, it seems to me that one such as this patient presents is the least responsive and most resistant to all forms of local or systemic treatment. It has been suggested that hidradenitis suppurativa might respond to the drugs of the sulfanilamide group. I think, however, that these drugs do not have any effect on this condition.

DR. HIRAM MILLER, San Francisco: It is of interest that most examples of this disease are observed in obese, comparatively young women. For this reason endocrine products have been used in treatment but have not been found to be of value. Sulfanilamide and allied products have not been helpful. The only satisfactory treatment for the disease when it is of any appreciable extent is complete surgical removal of the affected parts. This patient has had her disease for three years. I believe that surgical therapy should have been resorted to two and a half years ago.

DR. H. J. TEMPLETON, Oakland, Calif.: If Dr. Miller's pessimism extends to the early stages of this disease, I cannot agree with him at all. I have successfully treated many patients with a typical form of the disease in an early stage with long series of filtered roentgen ray treatments and injections of staphylococcus toxoid.

DR. WILLIAM GOECKERMAN, Los Angeles: I did not see this patient, but the diagnosis is evidently established. Perifolliculitis abscendens et suffodiens and dermatitis papillaris capillitii are evidently fundamentally of the same nature. A laborious morphologic terminology for an infection with the staphylococcus or a mixed infection with the streptococcus, with a predilection for the cutaneous glands, is in all probability secondary to a systemic focus. The conception which I have entertained for years was emphasized to me rather strongly by a case presented by Dr. Nelson Paul Anderson in which all three conditions were present simultaneously. Only time will tell whether the drugs of the sulfanilamide group will prove effective in such cases. I should like to support Dr. Templeton's contention that these conditions can be treated effectively by conservative measures in the early stages. It is only for the advanced condition that drastic surgical measures are necessary. This should be emphasized in order that these conditions may be diagnosed early and not be managed as recurrent furuncles possibly over several years' time.

DR. A. J. GRECO (by invitation), Los Angeles: It seems to me that this patient has, in addition to the suppurating sinuses in the axillas, a suppurating sinus extending deep in each groin of three years' duration, which is inadequately accounted for by the diagnosis given. I wonder if a Frei test has been performed in this case.

DR. FRANKLIN BALL, Hollywood, Calif.: I am glad that Dr. Goeckerman mentioned the fact that the staphylococcus is frequently the causative agent in cases of hidradenitis suppurativa. I do not wish to deprecate the drugs of the sulfanilamide group, whose efficacious effect in many bacterial infections has, as is well known, been so good that they will probably come to be used more and more. But I feel that in hidradenitis suppurativa there is some other factor present which apparently does not allow these drugs to exert their full effect. What this deleterious factor may be is not known, but it would seem to me that it is something which has to do with the physiologic action of the apocrine glands.

Gumma of the Nose Resistant to Antisyphilitic Treatment. Presented by DR. C. RUSSELL ANDERSON, Los Angeles.

A. R., a man aged 50, had a chancre in 1927. He received intermittent inadequate antisyphilitic treatment up to June 1939, at which time a small nodule formed in the nasal septum. The nodule soon ulcerated and perforated the septum. He was again given antisyphilitic treatment, but the entire nose ulcerated regardless of the treatment. In March 1940, after large amounts of arsphenamine had been administered, the nose began to heal again, and it remained well until about July, when a relapse occurred. Since September the patient has been receiving heavy injections of arsphenamine (0.6 Gm.), bismuth subsalicylate, liver extract and vitamins and one course of malarial pyrexial therapy. The nose has healed remarkably during the past month. The patient has also gained 25 pounds (11 Kg.) in weight. There is now an absence of the bridge and septum of the nose. There is a sequestrum of a nasal bone, especially on the right. The Wassermann reaction of the blood has been consistently positive. Wassermann reactions of the spinal fluid have been negative. A Krajian stain of a microscopic section shows faintly staining spirochetes.

DISCUSSION

DR. IRVING BANCROFT, Los Angeles: Dr. Greco and I have carefully examined the histologic sections in this case and were not able to see Spirochaeta pallida. I wish to call attention to the fact that certain cells have transitional forms

which are spiral and which stain with silver. They are apt to be mistaken for S. pallida. The Krajian stain itself is excellent, but the interpretation may be false in cases of late syphilis.

Dr. A. J. Greco (by invitation), Los Angeles: The clinical diagnosis in this case is obviously gumma of the nose or so-called malignant syphilis. However, the interpretation of the Krajian stain of the histologic sections presented is important because it seems that pathologists of equal repute cannot duplicate the results. I am sure that the Fontana method of staining smears for spirochetes is familiar. When a smear is made of the serum from a chancre and stained by the Fontana method, no doubt is left in the mind of the examiner if the smear is positive, because the spirochetes are distinct and it is even possible to actually count the number of spirals in the organism. Furthermore, the stained spirochetes are seen to have a clear halo around them. Similarly, with the Levaditi method of staining spirochetes in tissues, no doubt is left in the mind of the examiner when he sees the stained organisms. Dr. Bancroft and I examined the section of tissue from this case stained by the Krajian method with an oil immersion lens, and I can state definitely that I saw no structure which resembles the S. pallida as seen by the Fontana or by the Levaditi method.

Dr. N. P. Anderson, Los Angeles: Since Krajian's stain seems to be under attack, I arise to its defense. Every time that I have examined a slide stained by the Krajian method—and there have been many—I have noted the correctness of Mr. Krajian's observations as to the presence or absence of S. pallida. Naturally this stain is one of Mr. Krajian's favorites, and so he probably recognizes the presence of spirochetes many times when other people fail to see them. This procedure is one of great value and should be more widely used.

Dr. Stanley Chambers, Los Angeles: I should like to rise emphatically in the defense of the Krajian stain. It is very accurate.

Dr. C. Russell Anderson, Los Angeles: I should also like to come to the defense of the Krajian stain for spirochetes in tissue sections. At the Los Angeles County Hospital it has been found most satisfactory, and I deplore the fact that in other sections of the United States the use of it has not been adopted. In order to obtain good results (as with all staining methods) it is necessary to follow Mr. Krajian's technic exactly.

Dr. Howard Morrow, San Francisco: This patient reminds me of a physician that I treated thirty-three or thirty-four years ago. He had a malignant syphilid of the nose and nasopharynx. His syphilis developed from an extragenital chancre on his finger. There was great destruction within his nose, and he did not respond to mercury or iodide therapy. About this time arsphenamine first appeared on the market. The physician received the first injection of arsphenamine to be given in California and improved rapidly under the administration of weekly injections. He received thirty or forty injections of arsphenamine, and the lesions healed completely. He practiced medicine for thirty years and died just a short time ago.

Dr. N. N. Epstein, San Francisco: I agree with the clinical diagnosis of malignant syphilis in this patient. I suggest that the lesions be controlled by the combined simultaneous use of artificial fever and an arsenic preparation such as neoarsphenamine. It seems that more recent investigation would indicate that certain drugs are many times more effective when the temperature of the patient is elevated. Certainly, this is true of the sulfanilamide group of drugs. However, in this particular patient the lesions seem to be well under control at this time. I should like to see that principle employed should problems of this sort be encountered in the future.

Dr. C. Russell Anderson, Los Angeles: The gummous destruction of the entire nasal structure in this patient is the most extensive that I have ever seen. The process at first was recalcitrant to treatment with arsphenamine and heavy metals. It was only after the use of malaria, followed by massive doses of ars-

phenamine, bismuth and iodides and weekly intravenous injections of typhoid vaccine, liver extract given intramuscularly and by mouth, large doses of vitamin concentrates, repeated small blood transfusions and daily universal exposure to radiation from a quartz mercury vapor lamp that the progressive destruction was stopped. As can be seen, healing is almost complete and the patient has gained weight and feels and looks well. I believe that this patient owes his life to the sum total of everything used and not to any one single part of the therapy.

LOS ANGELES DERMATOLOGICAL SOCIETY

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March 11, 1941

A Case for Diagnosis (Pemphigus? Senear-Usher Syndrome?). Presented by DR. THOMAS NESBIT.

J. C. F., a man aged 35, states that an eruption first appeared on his left shoulder several years ago. The lesions have been completely healed at times, but new ones have developed in the same area. He has been under treatment during the past year without any change in the lesions. Circinate, crusted, superficially ulcerated areas about 1 cm. in diameter surrounded by scattered small vesicles are on the back of the neck and on the left shoulder. A positive Nikolsky sign was elicited in the skin around the lesions. The microscopic examination showed several flattened vesicular spaces in the epidermis. In one place there was a denudation of the epithelium. The cutis showed a moderate engorgement of the blood vessels and a small infiltration of polymorphonuclear leukocytes and round cells. No blastomycetes were present. The pathologic diagnosis was "chronic inflammatory changes."

DISCUSSION

DR. N. P. ANDERSON: I think that this case is one of benign familial pemphigus, as described by Hailey and Hailey (Familial Benign Chronic Pemphigus, ARCH. DERMAT. & SYPH. **39**:679 [April] 1939). In Baltimore the condition would be considered to be Darier's disease with vesiculation (Fels, I. R., and Goodman, M. H.: Criteria for the Histologic Diagnosis of Keratosis Follicularis [Darier], ibid. **39**:438 [March] 1939). In Los Angeles the same entity has been recognized (Ayres, S., and Anderson, N. P.: Recurrent Herpetiform Dermatitis Repens, ibid. **40**:402 [Sept.] 1939). I believe that this disease is a definite entity both clinically and histologically. The histologic observations are so characteristic that I believe a diagnosis can be made by microscopic studies alone. This suggestion was first made by me several months ago. At the coming convention of the American Medical Association in Cleveland Drs. S. B. Frank and C. R. Rein are to present a paper on the same disease but under the title of "Dyskeratoid Dermatosis" (this issue, p. 129). Just where this disease should be classified appears to be open to discussion. I believe that it does not belong in the same group as Darier's disease. One should always hesitate before attempting to present a new disease entity and ask the question, "What was this condition previously called?" Competent dermatologists have been studying cutaneous conditions for at least seventy years. What did they call such conditions years ago? Incidentally, some months ago while looking through one of the old issues of the *American Journal of Medical Sciences,* I found a case report by Dr. Louis A. Duhring in which a similar condition was described. Duhring stated the belief that the condition in his particular case was a fungous infection. The quality of photographic reproduction was rather poor years ago, and it is difficult to tell from photomicrographs

and the clinical picture whether Duhring was describing the aforementioned entity. Dr. Samuel Becker, of Chicago, has the largest series of cases of this kind, numbering between 50 and 60, in which the familial character has been most striking. I believe that his patients all belonged to a certain French-Canadian group who had long since given up consulting doctors because they felt that the disease was just as much a part of them as the texture of their skin or the color of their eyes. I have been surprised that except for the aforementioned cases no comparable ones have been described in the literature in English, French or German. One always wonders just what conditions were called before somebody tried to give them new names. Incidentally, the case that Dr. Halloran presented a couple of months ago was also a typical instance of this disease. The microscopic picture in this case was characteristic. Secondary infection does occur in Darier's disease. The latter disease is familial, and at times in mild form it appears and disappears. Both Dr. C. Russell Anderson and I have presented cases of proved Darier's disease in which there had been total disappearance of the lesions at times. It is interesting to note in going through the French literature dealing with the various cases of Darier's disease that have been presented in France that a great many were observed by Darier himself, who at least should have been able to recognize his own entity. However, there has never been any condition described such as this patient presents. It certainly would seem, considering all of the cases of Darier's disease that have been presented during the past forty years, that some cases would have been described in which this picture was presented. Impetiginous lesions have been described, but the peculiar picture of a spreading undermining herpetiform eruption has not to my knowledge been described before 1939.

DR. WILLIAM GOECKERMAN: I visited Dr. Kren's clinic in Vienna in 1937. He presented a number of cases of this type and called the condition pemphigus vulgaris in contrast to pemphigus vegetans or pemphigus foliaceus. This type of pemphigus vulgaris was considered a comparatively benign form. My own opinion is that pemphigus and lupus erythematosus are definite disease entities but that at a given time it may be impossible to differentiate them by morphologic and histologic examination. In time the differentiation becomes definite. Lupus erythematosus, the chronic as well as the acute form, is always systemic and not local. I believe that one sees all gradations from the most indolent to the most acute types. But one must recall that the cause of neither pemphigus nor lupus erythematosus is known.

DR. N. P. ANDERSON: I think that there is such an entity as Senear-Usher pemphigus. There are conditions which simulate lupus erythematosus, conditions which simulate seborrheic dermatitis and still others which are more or less closely related to pemphigus both in clinical appearance and in the eventual fatal outcome. I think that the acceptance of this entity by a dermatologist such as Dr. Udo Wile, of Ann Arbor, Mich., is significant. This syndrome is of relatively recent recognition, as the original paper was published in 1926 (Senear, F., and Usher, B.: An Unusual Type of Pemphigus Combining Features of Lupus Erythematosus, ARCH. DERMAT. & SYPH. **13**:761 [June] 1926). Wile and Arnold (The Senear-Usher Syndrome, ibid. **40**:687 [Nov.] 1939) concluded that the disease is a definite entity distinguishable from lupus erythematosus, pemphigus vulgaris and pemphigus foliaceus.

Purpura Haemorrhagica. Presented by DR. A. K. JENSEN.

E. H., a white man aged 40, states that about seven months ago he noticed small purplish spots developing on his legs and thighs. Palm-sized, well marginated, desquamating lesions on the anterior surface of the right leg appeared later. Both legs and thighs now show scattered pinhead-sized to dime-sized purpuric lesions. The patient has taken three bottles of "three S tonic" and some Chinese herb medicine. The examination of the blood showed the following results: erythrocytes, 5,270,000; platelets, 156,000, and vitamin K prothrombin time, 64 per cent. A tourniquet test for vitamin C deficiency gave a positive reaction. The

patient has received vitamin K, caroid and bile salts, pills of ferrous carbonate U. S. P. calcium gluconate intravenously and autogenous whole blood intramuscularly. At present he is receiving ascorbic acid intravenously.

DISCUSSION

DR. BEN A. NEWMAN: Obviously this condition is not purpura haemorrhagica, if by that name is meant thrombopenic purpura. This patient's lesions are simple or symptomatic purpura.

DR. A. F. HALL: I should think that without any laboratory examination and only by considering the distribution of the lesions one should suspect that the condition in this case is that type of purpura which is due to fragility of the blood vessels. The patient had no lesions above the middle of his thighs. He had never had any purpuric or hemorrhagic manifestations other than in the skin.

Lupus Erythematosus Resistant to Treatment. Presented by DR. SAMUEL AYRES JR.

B. D., a woman aged 32, states that her present illness began about three years ago with a slight itching and redness on the right cheek. The eruption has continued to spread in spite of various types of treatment. The patient was first examined on Oct. 3, 1940, at which time the eruption was similar to that now seen. Prior to her first visit the patient had received a total of twenty-eight intravenous injections of gold sodium thiosulfate as well as intramuscular injections of bismuth subsalicylate. Quinine and sulfanilamide had also been administered. None of these medicaments were beneficial. Under the present regimen the patient has received five intravenous injections of gold sodium thiosulfate, the largest dose being 30 mg. The patient complained of pruritus after each dose of gold and stated that she had a similar experience when receiving this compound previously. The gold therapy was therefore discontinued. She then received four intramuscular injections of bismuth subsalicylate and, more recently, eleven intramuscular injections of liver extract (Lilly), the dose being 0.5 cc. at approximately five day intervals. The eruption has continued to spread in spite of these measures. At present the lesions involve the medial portion of the cheeks and forehead, with small areas on the alae of the nose and on the right upper eyelid. In some places the lesions have indistinct borders but in others they are fairly well defined. All the lesions are superficial and erythematous and show slight scaling and stippling. There is practically no infiltration. The patient is presented for therapeutic suggestions.

DISCUSSION

DR. KENDALL FROST: At the Los Angeles General Hospital a few patients with lupus erythematosus who were resistant to treatment have been given a high vitamin intake and liver intramuscularly. They have shown considerable improvement following the institution of these measures.

DR. BEN A. NEWMAN: This patient presents several blotches of persistent erythema on her face conforming to the clinical picture of superficial lupus erythematosus. On being questioned the patient presented some pertinent facts in her history. She has been told on several occasions that she has a heart murmur. Several years ago she had some type of kidney disease which was believed to be due to calculi. For the past year or more she has been aware of a slight daily fever varying from 99 to 100.5 F. Her condition probably belongs to the same group of conditions as lupus erythematosus with associated visceral involvement, i. e. the Libman-Sachs syndrome. I suggest that further studies he made, including a test of renal function and determination of the presence of valvular cardiac lesions.

DR. H. C. L. LINDSAY: The members of this society may have noticed an article concerning the successful treatment of lupus erythematosus by means of sulfanilamide (Anderson, H. F.: Fulminating Acute Lupus Erythematosus Cured by Sulfanilamide, ARCH. DERMAT. & SYPH. **38**:621-622 [Oct.] 1938).

Lupus Erythematosus Complicated by a Fungous Infection. Presented by Dr. H. C. L. Lindsay.

P. S. T., a Montenegrin aged 55, states that a scaliness first appeared on the bridge of his nose during an attack of hay fever in 1936. This eruption spread to the tip of the nose and face about six months ago. The patient has received roentgen ray treatments of 15 r each and a total of forty-two intravenous injections of gold sodium thiosulfate. Examination now shows scattered erythematous dime-sized to dollar-sized plaques on the nose, ears and cheeks. The plaques show atrophy, scarring, telangiectasia and scaling. The Wassermann reaction of the blood was negative. The urine was normal. Cultures from scales showed a fungus with branching hyphae on the tenth day.

DISCUSSION

Dr. Samuel Ayres Jr.: I could not see any lesions that suggest a fungous infection. The eruption appears to be a typical lupus erythematosus.

Dr. H. C. L. Lindsay: This patient came to me with a diagnosis of lupus erythematosus made by several reputable dermatologists. Anterior to the left ear was a dollar-sized area that resembled a fungous infection. Scales were removed from this area and examined by the laboratory technician. Cultures showed a fungus that has not been identified.

Dr. Saul S. Robinson: I saw this patient five years ago with an initial lesion of lupus erythematosus on the tip of the nose. The lesion was clinically a lupus erythematosus. The response of the lesions was favorable to treatment with gold and freezing with solid carbon dioxide. I did not see him again until this meeting. It is my opinion that he has still a lupus erythematosus which has spread over the face and ears. I did not see any lesions that would change my original diagnosis.

Dr. H. P. Jacobson: This patient reminds me of one I saw who had a lesion of the upper lip which was a typical tertiary syphilid. He had a laboratory examination of the lesion, and a diagnosis of fungous disease was made. I do not mean to infer that the condition in this case just presented has any resemblance to a tertiary syphilid. There is danger in seeing fungous elements in lesions and in believing that the lesion is caused by the mycelium or elements resembling mycelium observed under the microscope. This patient has a photosensitive dermatitis. The patient also has an involvement of the lower lip. I believe that the fungus observed under the microscope here should not be given any serious consideration. This condition is not a fungous disease; it is a photosensitive dermatitis.

Urticaria Pigmentosa. Presented by Dr. Samuel Ayres Jr.

W. S., a man aged 33, has a history of an eruption that appeared on the right forearm about three or four years ago and slowly enlarged. The eruption was associated with itching and burning sensations, especially after the skin was rubbed or irritated. The patient believes that certain foods, particularly ice cream and highly seasoned foods, aggravate the eruption. No treatment has been given. The lesions are now widely scattered over most of the body, with special involvement of the upper part of the trunk, the neck, the arms, the groins and all aspects of the feet. The eruption is of a mottled appearance and in the worst areas consists of pea-sized to bean-sized brownish freckle-like lesions which do not appear to be elevated. When the skin is rubbed the lesions become definitely elevated and slightly erythematous.

DISCUSSION

Dr. Max J. Wolff: I agree with the diagnosis of urticaria pigmentosa. The case is somewhat unusual in that the duration of the disease is only about three years. The lesions are not quite typical, yet I think that if a histologic examination was done it would probably confirm the diagnosis.

Dr. H. C. L. Lindsay: Urticaria pigmentosa is easy to diagnose in this instance. Irritation of the papules elicits a so-called erection of the papules.

Urticaria pigmentosa must be distinguished from syphilis and xanthoma. A certain degree of success in the treatment of urticaria pigmentosa is obtained by the oral administration of minute doses of mercury bichloride.

A Case for Diagnosis (Contact Dermatitis?). Presented by DR. MAX J. WOLFF.

E. G. R., a man aged 23, had an eruption on his face, eyelids, cheeks and neck which developed about two and one-half months ago. One day prior to the onset of the eruption the patient had a hair tonic rubbed into the scalp. Although the application was not repeated, periods of remission and exacerbation in the eruption have since been present. Patch tests with a hair tonic and with a cologne gave negative results. There is now an ill defined erythematous eruption on the face, eyelids, neck, cubital fossae, arms and wrists.

DISCUSSION

DR. N. P. ANDERSON: I think that this condition is one of those nondescript eczematous eruptions which is mostly localized around the face, ears and neck, with a few patchy areas on the arms. I believe that Dr. Wolff has made the correct diagnosis, namely, contact dermatitis. I think that the difficulties in proving that this is the correct diagnosis are sometimes insurmountable. Most difficulties in diagnosis have to do with the cooperation of the patient. I have often wondered just how these lesions arise on the arms and forearms. One conception is that the patient sometimes transfers the irritant directly from the scalp or indirectly through the use of the hands by touching various places on the arms. Many people sleep with the hands above the head, and as they turn the head from side to side they occasionally place the irritant in contact with the arms and forearms. I think that the main difficulty in proving a diagnosis of this type lies in the fact that most patients are convinced that they have an "acid" eruption or some other type of eruption far removed from what the dermatologists think it to be.

DR. SAUL S. ROBINSON: I should like to make a suggestion in this case, especially since a contact dermatitis is simulated and no causative agent can be found, namely, that a diagnosis of neurodermatitis be considered. Neurodermatitis in the disseminated form can involve the eyelids, the neck and the extremities and can simulate a dermatitis caused by an external irritation. I suggest that Dr. Wolff treat the patient for a neurodermatitis, provided no success is otherwise obtained in clearing the condition, and present him at later meeting.

DR. H. C. L. LINDSAY: In every case of apparent neurodermatitis the scales should be examined microscopically. Lesions which look like neurodermatitis may prove to be a fungous infection. I agree with the presenter's diagnosis.

H. C. L. LINDSAY, M.D., *Chairman*

SAUL S. ROBINSON, M.D., *Secretary*

April 8, 1941

Lichen Sclerosus et Atrophicus. Presented by DR. SAUL S. ROBINSON.

L. H., a white woman aged 43, states that for several months an itching area has been present on the right scapular region. There is a palm-sized whitish indurated slightly elevated papular and atrophic plaque on the right scapular region with a stippled surface. Comedo-like plugging is seen throughout the involved area. Examination showed the blood and urine to be normal. The basal metabolic rate was —9 per cent. The histologic picture was typical of lichen sclerosus et atrophicus.

DISCUSSION

DR. N. P. ANDERSON: There is nothing from either a clinical or a microscopic standpoint to suggest or uphold the diagnosis as presented. In every case of lichen sclerosus et atrophicus that I have ever encountered comedo-like plugging has been a prominent clinical feature. I did not see any plugging in the large plaque presented by the patient.

DR. SAUL S. ROBINSON: I thought that the centers of the plaque showed this feature well.

DR. C. R. ANDERSON: I think that the plugging is well brought out. I think that the diagnosis is lichen sclerosus et atrophicus. I have seen 1 patient with this condition in whom involution of the lesions was obtained by giving mercury bichloride intramuscularly as in the treatment of lichen planus. I believe that there is a relation between the two diseases and that they probably are one and the same disease.

Ehlers-Danlos Syndrome. Presented by DR. N. P. ANDERSON.

E. H., a Mexican girl aged 11 years, has had scars on the face, arms and legs since she was 1 year of age. She presents a definite Ehlers-Danlos syndrome with numerous papyraceous scars involving the extensor surfaces of the knees and the lower part of the legs. There are occasional scars on the lateral surfaces of the thighs and linear scars on the forehead. The patient also presents hyperextensibility of all the joints and a moderate cutis laxa. No spherules are present.

DISCUSSION

DR. H. C. L. LINDSAY: On palpation of the skin of a patient suffering from the Ehlers-Danlos syndrome there is a softness in the texture beyond visible lesions and unlike that felt in the normal skin.

Nevoxanthoendothelioma. Presented by DR. N. P. ANDERSON.

S. C., a boy aged 28 months, has an eruption on the temple, under the chin, in the ear and on the trunk. The lesions were first noticed when the child was about 1 month old and appear to be growing. There are multiple solitary, split pea–sized and smaller yellowish xanthomatous tumor masses scattered as described. The sugar content of the blood was 81.08 mg. per hundred cubic centimeters, and the cholesterol content was 152.9 mg.

DISCUSSION

DR. M. J. WOLFF: Is it not rather unusual to find comparatively low sugar and low cholesterol values in the blood?

DR. N. P. ANDERSON: "Nevo-Xantho-Endothelioma" was the title of the paper written by McDonogh in 1912 (*Brit. J. Dermat.* **24**:85, 1912). McDonogh did not realize at the time that juvenile xanthoma is divided into two types. The common type of juvenile xanthoma presents xanthomatous lesions on the buttocks and other points of pressure. With nevoxanthoendothelioma lesions occur on the upper half of the body, that is, the upper part of the trunk, the face, the neck and the scalp. The latter type is associated with normal blood sugar and cholesterol values, and eventually the lesions disappear spontaneously, leaving scars. This diagnosis, of course, can be substantiated only by microscopic examination of a piece of tissue.

A Case for Diagnosis (Persistent Pityriasis Rosea? Parapsoriasis?). Presented by DR. SAUL S. ROBINSON.

A. B., a white woman aged 40, states that an eruption appeared about three years ago on her trunk and in the axillas and groins. There is no history of the ingestion of drugs. A slight pruritus is associated. There are discrete round and

oval scaling maculopapular lesions varying in size from that of a pea to that of a half-dollar on the trunk and in the axillas. The Wassermann and Kahn reactions were negative. The blood count and the urine were normal. The lesions have been resistant to all types of therapy.

DISCUSSION

DR. C. R. ANDERSON: I do not know what to call this condition, which has a peculiar distribution. I think that a diagnosis of intertrigo must be seriously entertained, but the appearance of the eruption is certainly not typical of intertrigo. The distribution of the eruption leads me to believe that some article of clothing may have something to do with the causation. I asked the patient what kind of brassiere she wore but could not secure any information. The eruption is both beneath and about the undersurface of the breasts, about the axillas and in the inguinal creases. Such a disease lasting for three years with little response to therapy makes me believe that there has been some other element that has been overlooked.

DR. SAUL S. ROBINSON: The first conditions that were ruled out in this case were a contact dermatitis and a fungous infection. There has been no response of the lesions to any form of therapy, including the coal tar preparations. I think that this eruption may be a manifestation of an internal focus of infection. An allergic condition of the skin secondary to a staphylococcic infection should be considered. I was thinking of administering sulfathiazole and staphylococcus toxoid. The eruption may belong to the group of staphylodermas.

Lichen Planus Developing in a Patient Under Treatment for Syphilis. Presented by DR. ANKER K. JENSEN.

A. N., a man aged 50, has had cutaneous lesions on the right leg for the past two years. About six months ago scattered lesions also appeared on the thighs and arms. The lesions begin as small discrete papules that coalesce and form larger areas. Numerous small lesions are flat topped, shiny, violaceous and pruritic. Most of the lesions are now located on the flexor surfaces of the extremities. The Wassermann reaction of the blood was negative. The microscopic picture was typical of lichen planus. Arsenical preparations for the treatment of syphilis have been administered.

DISCUSSION

DR. SAUL S. ROBINSON: I agree with the diagnosis. I examined the histologic section in this case, and I consider the microscopic observations to be compatible with the diagnosis of lichen planus. The question that arises is whether or not lichen planus can be caused by the drugs used in the treatment of syphilis. This patient has syphilis and was treated with bismuth and arsenic. Whether or not the lichen planus eruption caused by these drugs is identical to lichen planus developing in patients not receiving such drugs is an interesting problem.

DR. H. C. L. LINDSAY: The papules are exceptionally indurated for lichen planus, but cases have been observed in which lichen planus has developed after injections of neoarsphenamine.

DR. A. K. JENSEN: If a patient suffers from lichen planus, the treatment most likely to be administered would be injections of a bismuth compound. I know that bismuth is not a dangerous drug. Here is a man who has been receiving bismuth and neoarsphenamine therapy and in whom lichen planus develops. The problem here is a therapeutic one. I should like to know what drug to use to continue treating the syphilis.

A Case for Diagnosis (Erythema Annulare Centrifugum?). Presented by DR. M. J. WOLFF.

A. G. F., a man aged 40, about three months ago first noticed an eruption on his left cheek. The examination shows an oval, circinate dull red lesion on the

left cheek. The border of the lesion is firm and elevated, and in places it is covered with fine scaling. The center of the lesion is smooth and dull red. The blood and the urine were normal when examined.

DISCUSSION

DR. C. R. ANDERSON: I think that this lesion is lupus erythematosus.

DR. WALTER SCHWARTZ (by invitation): I thought of the diagnosis of lupus erythematosus, but I usually wish to see atrophy in order to make this diagnosis. As far as granuloma annulare centrifugum is concerned, I thought that it was more or less a generalized disease with several lesions in widely distributed parts of the body. I favor the diagnosis of granuloma annulare.

DR. SAUL S. ROBINSON: My diagnosis is granuloma annulare. I should like to see this patient presented again after treatment is instituted.

DR. A. F. HALL: I think that the center of this lesion is definitely not normal skin. It is pale and possibly atrophic. The patient said that he painted tincture of iodine on it, and since that time it has been paler than normal. I do not believe that the patient is giving a true history of the evolution of the lesions. In view of the dilated and plugged follicular orifices in the border, my diagnosis would be lupus erythematosus.

DR. N. P. ANDERSON: I do not recall any disease that involves the malar regions of the face and has dilated follicular orifices that is not lupus erythematosus.

DR. M. J. WOLFF: The three diagnoses that occurred to me are the conditions just discussed. I favored first the diagnosis of erythema annulare centrifugum and last that of granuloma annulare. There was some scaling on the edge of the lesion, and I could not see any definite atrophy in the center.

Herpes Zoster Associated with a Generalized Varicella-like Eruption. Presented by DR. MAX J. WOLFF.

M. S., a Polish Jew aged 68, about five years ago felt an "itching" on the back of his neck that was followed two days later by an eruption. New lesions appeared elsewhere on the body one or two days ago. Examination shows groups of vesicles on an erythematous base on the back of the neck extending to the hair line and to the right of the midline, on the right shoulder and in the right pectoral region. There are discrete match head–sized vesicles on the right arm and forearm. One vesicle is on the lumbar region to the right of the midline, and a few vesicles are on the abdomen and on the left arm and forearm. There is axillary adenopathy on the right side.

DISCUSSION

DR. SAUL S. ROBINSON: I agree with the diagnosis as presented, and I believe that this patient has a generalized type of herpes zoster with varicella-like lesions. I have had a similar case of this condition with the same distribution, that of an elderly patient, and I should be interested to learn whether or not a postzoster neuralgia occurs later in this patient.

DR. N. P. ANDERSON: I suggest that this patient have a blood count made and a thorough physical examination for evidence of a possible lymphoblastoma. In many cases of severe herpes zoster the condition is associated with a lymphoblastoma.

DR. WALTER SCHWARTZ (by invitation): Recently, a well known pharmaceutic company has been showing a motion picture concerning the benefits derived from the use of smallpox vaccine in the treatment of herpes zoster. Several of the oculists have spoken to me about this type of therapy and are enthusiastic about it.

Localized Scleroderma. Presented by DR. N. P. ANDERSON.

I. G., a girl aged 12 years, has had a "spot" on her shoulder for about eight and one-half years. A similar condition has been on a finger about the same length of time. The lesions are increasing in size. On the left hand is a thickening along

the medial side of the thumb with a thinning of tissue and contracture of the middle finger laterally toward the little finger. On the right hand is an atrophy of the skin of the middle finger over the dorsum of the last phalanx and over the knuckle. The left side of the upper part of the chest shows three pigmented areas, two the size of a dime and one the size of a half-dollar. The center of these lesions is white and atrophic. The left forearm is smaller than the right. A roentgenogram of the left hand revealed an ulnar deviation of the distal phalanx of the middle finger associated with an oblique articulation of the margin of the middle phalanx just proximal to this point.

DISCUSSION

DR. BEN A. NEWMAN: The atrophic hardening of the skin which this patient presents on her finger is not the usual conception of scleroderma, especially with the absence of scleroderma or morphea elsewhere on the body. However, the symmetry of these lesions on both hands makes one suspect that it is more than a coincidental observation. I noted that the patient has no pulse in the left wrist. Is it possible that there may be some neurologic disorder producing this atrophy? This patient should be investigated for such abnormalities as cervical ribs or a tumor or malformation affecting the brachial plexis or upper thoracic vertebrae.

DR. A. K. JENSEN: I believe that this patient has an atrophy of the skin.

DR. N. P. ANDERSON: I have never observed a similar case of scleroderma.

A Case for Diagnosis (Dermatitis Factitia?). Presented by DR. SAMUEL AYRES JR. and DR. N. P. ANDERSON.

N. F., a girl aged 16, states that her eruption first appeared in May 1938 and persisted for about six weeks. The patient was then free of lesions for nearly two years until the eruption recurred with numerous attacks between May and November 1940. There was then a period of freedom from lesions between November and January 1941. Since January 1941 the patient has been having almost continuous attacks of the eruption. With the exception of two areas of involvement, all of the lesions have occurred on the left leg or left arm. All of the lesions develop during the night. The patient's referring physician stated that the lesions continued to appear when the patient was hospitalized and under close supervision and even when the involved skin was well covered with bandages. At the time of the patient's visit, on April 14, 1941, she presented an eruption scattered over the left leg and the left hand and forearm, where there were a number of square dollar-sized superficial lesions. Some of the lesions showed superficial scars, and others showed dried scales and crusts. On the medial aspect of the right ankle was a fresh bullous lesion which the patient stated began about five days previously. Scratch and intradermal tests by an allergist showed the patient to be sensitive to a large number of allergens. The patient also gave positive transfer reactions to a number of foods. The allergist stated that there did not seem to be much correlation between the sensitivities observed and the appearance of the cutaneous lesions.

DISCUSSION

DR. M. J. WOLFF: I think that the lesions on the left side of the body would be accessible to the right hand. Usually the lesions appear at night, the patient awakening suddenly and finding them. It is probably difficult to determine the exact cause of the eruption.

DR. H. C. L. LINDSAY: I had a "neurotic" patient who could produce lesions on her back. She fooled her physician for a long time. She had a small bottle of phenol with a large cork. She would put the dipped cork on the wall and back up to it. The lesions were perfect circles and were of uniform size. Another girl produced an ulceration on her wrist, with escharotic chemicals, that was so large that one could see all the tendons. Her physician, who referred her to me, was later able to get a confession from her as to the cause of the lesions.

DR. M. J. WOLFF: A patient whom I suspected wanted to avoid the draft. The lesions on his legs were sharply defined and square angled, as if the irritant had been mustard plasters.

DR. WALTER SCHWARTZ (by invitation): There is one correction in the history. Dr. Ayres stated that these lesions continued to develop under a bandage while the patient was in the hospital. This knowledge was not a result of his own observations but was obtained from the patient's history. If an occlusive bandage is applied, the best one is probably one made with hard paste of zinc oxide N. F. It is a frequent observation that patients with this condition have a loss of the pharyngeal reflex; I wonder if this is a consistent observation. If one finds that such a patient produces his own lesions and stops him, what will he do next? Does such a patient have hysteria?

DR. A. F. HALL: It will often result in the development of other symptoms as an emotional outlet.

A Case for Diagnosis (Acne Vulgaris?). Presented by DR. SAMUEL AYRES JR.

W. R. T., a woman aged 20, has an eruption on the face, chest and back that first appeared about five years ago. She received two series of roentgen ray treatments administered by dermatologists. The patient had been taking 2 grains (0.13 Gm.) of thyroid a day for two years at the time of her first visit, in July 1940. She admits that she excoriates the lesions. The lesions consist almost entirely of scattered superficial crusted and excoriated papules. There are a few small pustules. No comedos are present. Cultures have grown only Staphylococcus albus. Routine scratch tests with foods have given negative reactions. The patient has had a series of injections of autogenous vaccine as well as ultraviolet irradiation and the application of solid carbon dioxide with sulfur.

DISCUSSION

DR. A. F. HALL: I do not believe that this patient has ordinary acne. I do not know whether there is an external irritating factor, such as hair dye, which she claims to have used only in recent months, or a psychic factor. There are certainly excoriations present, but they seem to be so symmetrically distributed that I should not be satisfied with the diagnosis of neurotic excoriations. I believe that this condition is an acneform eruption with seborrheic distribution, but I am not satisfied with any diagnosis that I can make at this time.

DR. N. P. ANDERSON: I wonder if any of the members have ever seen a patient with acne that has been aggravated by the ingestion of iodized salt. I think that occasionally such an event takes place, but it is extremely rare. Iodides and bromides administered therapeutically are frequent offenders, but I have never encountered a case in which I could actually say that the condition had been made worse by the taking of iodized salt.

DR. HERBERT LAWRENCE (by invitation): The patient told me that she can see the lesions, and she is industrious about carefully picking at the lesions on her face. She is not comfortable until the lesions are removed.

Dermatitis of the Face and Eyelids from Nail Polish. Presented by DR. C. R. ANDERSON and DR. HERBERT LAWRENCE (by invitation).

H. B., a woman aged 30, was first seen in August 1940 because of an acute vesicular dermatitis of the fingers, face and neck following the application of a cream containing merthiolate to the face and mercury bichloride soaks to the fingers. She had received this treatment because of a paronychia following a manicure and because of a dermatitis of the neck of one month's duration. The acute dermatitis quickly subsided and left a lichenified dermatitis on the eyelids and the right side of the neck, which gradually cleared with superficial roentgen ray treatment. The patient was well in October 1940. There was a recurrence

of the dermatitis of the eyelids, face and neck on Nov. 12, 1940, and the use of nail polish was ordered discontinued. On December 16 the patient was discharged as well. The patient did not use nail polish again for six weeks, and then its application was again followed by a recurrence of the dermatitis on the following day. Three weeks later another brand of nail polish was used, with a prompt recurrence of the dermatitis on the following day in the form of red and swollen eyelids. The dermatitis has now spread to the nose, cheeks and sides of the neck. Patch tests with the two brands of nail polish have given negative results. The examination today reveals redness, edema and scaling of the eyelids, cheeks and sides of the neck.

DISCUSSION

DR. A. K. JENSEN: This case shows that one may obtain a negative reaction to a patch test and still have a dermatitis that is definitely shown to be due to the test substance.

DR. SAUL S. ROBINSON: I disagree with the diagnosis in this case. As the reactions to patch tests with the nail polish have been negative, I suggest a diagnosis of neurodermatitis. This patient suffers from a severe pruritus in the involved areas. There is no evidence of vesiculation in these areas, such as is usually found in contact dermatitis. I questioned the patient regarding her occupation and living conditions. There is a psychic background here for the development of neurodermatitis, and it may be that if the patient is treated for neurodermatitis her eruption will clear.

DR. H. C. L. LINDSAY: A patient may have no reaction from a patch test with nail polish, but if during sleep she puts her hands under her face, then the moisture of the skin gives the dye time to act more effectively. The hands seem to have a certain amount of immunity to the dye. An article appeared last week about this type of dermatitis (Hollander, L.: Nail Laquer Dermatitis, *J. A. M. A.* **115**:1714-1715 [Nov. 16] 1940). Eosin in the dye may be the causative factor.

DR. M. J. WOLFF: I have observed a number of cases of this condition, but in all of them patch tests always elicited positive reactions.

DR. H. C. L. LINDSAY: I had a patient not long ago who had a dermatitis on the face, neck and arms. Patch tests with nail polish gave negative results. This patient had been under observation for years by an allergist. I thought that the eruption was due to contact with an irritant. The only two possible irritants that were missing in the long list of substances tested were lipstick and nail polish. The patient found out within three weeks that her rash appeared while she was taking nail polish off. I believe that the acetone polish remover was causing the lesions. Since she stopped using the nail polish the eruption has not recurred.

DR. A. F. HALL: I should like to say a few words regarding the use of patch tests for the detection of nail polish irritation. In the few cases that I have examined positive reactions were elicited, usually only mildly positive. In fact, the reactions were so mild that I thought that some of the color was still adhering to the skin because there was no vesiculation or papular reaction. I was told by a patient who is in the cosmetic-manufacturing business that there are three basic types of lacquer used in the commercial brands of nail polish. I was puzzled about the significance of mild positive reactions to patch tests in some cases; so my office nurse gave herself patch tests with eight different brands of nail polish, two of which, representing two basic types of lacquer, gave very mild positive reactions. She then started to apply one of these brands to see if a dermatitis would develop but never applied it regularly. At the end of about eight or nine days she thought that she felt an itchiness on her eyelids, and on the fourteenth day there was definite pinkness, swelling and scaliness of the eyelids. Regarding Dr. Anderson's case, I think it would be interesting to have the patient try two brands of nail polish representing two basic types of lacquer after a patch test to see if she gets a recurrence of her dermatitis after using the third type of lacquer.

Pemphigus of the Mucous Membrane. Presented by DR. W. F. SCHWARTZ (by invitation).

L. C., a man aged 71, during the past seventeen months has been having transitory superficial ulcers on the mucous membranes of the mouth and on the penis. Each lesion begins as a flaccid-topped bleb which ruptures within a day or two and leaves a superficial denuded area usually with a clean base. Occasionally the base of the lesion is covered with a friable white membrane. There is never any apparent infiltration or inflammatory reaction beneath or surrounding the ulcer. Each ulcer usually heals within ten to fourteen days without leaving a scar. The pain is usually intense. Most of the ulcers have ranged in size from 4 to 8 mm., but on two occasions ulcers on the inside of the cheeks have been 3 cm. in diameter. The soft palate is the site most frequently affected, although numerous lesions have appeared on the inside of the cheeks and under the tongue. The dorsum of the tongue, the lips and the conjunctiva of the eyes have exhibited no lesions. The glans penis almost constantly has similar lesions. The patient always has been in good health and even now feels well except for the pain in the mouth. At no time have there been cutaneous lesions. One set of complete upper and lower artificial dentures was worn for twelve years prior to the onset of the oral ulcers, but these have not been used since. The patient has been seen by many internists, and the only significant clinical or laboratory observations have been a basal metabolic rate of —20 per cent and a reduction in the free hydrochloric acid in the gastric analysis. Two complete blood counts done in the past year showed essentially normal values except for a slight eosinophilia, there being 5 and 4 per cent eosinophils. A smear from the mouth revealed no Vincent's spirochetes. The serum calcium was 10.8 mg. per hundred cubic centimeters and the serum phosphorus 3.2 mg. A microscopic examination of tissue from the margin of an ulcer was reported as showing merely "chronic inflammation."

DISCUSSION

DR. SAUL S. ROBINSON: I suggest that the possibility of a drug eruption be considered, as the lesions are present in the mouth and on the penis, which are favorite sites for drug eruption. One especially must rule out phenolphthalein. The patient states that he had been taking "O.M. tablets" on the average of 1 tablet a day for a considerable length of time.

DR. C. R. ANDERSON: I think that there is some possible indication for the diagnosis of phenolphthalein eruption.

DR. WALTER SCHWARTZ (by invitation): I had considered the possibility of a drug eruption, and the patient has been advised not to take any drugs other than the ones that I ordered for him at the dispensary. I was much chagrined to find out that he had been taking some O.M. tablets. I was interested to learn the phenolphthalein content of these tablets, and on inquiry a pharmacist said that there is no phenolphthalein in them. They contain mandrake, cascara sagrada, aloin and extract of belladonna. He has been taking these tablets at intervals for the past seven years. This eruption has been present only for seventeen months.

DR. H. C. L. LINDSAY: I agree with the diagnosis of pemphigus. This disease may involve the mucous membranes of the mouth and of the penis. This particular type usually is not so rapidly malignant as other types, since some patients with it live for seven or eight years. Lesions in pemphigus often confine themselves to the mucous membrane of the mouth, penis or vulva.

DR. WALTER SCHWARTZ (by invitation): Pemphigus of the mucous membranes is apparently recognized as a distinct entity, but I have heard authorities state that they did not approve of this diagnosis because there is no relation to pemphigus vulgaris. At present I have 2 other patients with the disease under my observation. The patient presented tonight and 1 other are past 60 years of age. I mention the age to see if one can elicit a common denominator among these cases. All 3 patients have had the lesions in their mouths since they have been wearing

dental plates. All 3 of them have worn complete dentures and are not now wearing them, but the ulcers continue to appear. The other suggestive common denominator is that the patients have passed the menopause age. I do not necessarily for the diagnosis of pemphigus of the mucous membranes. I have never observed a case in which the condition has progressed to the pemphigus vulgaris stage. But for lack of a better diagnosis, I am afraid that I must make the diagnosis of pemphigus of the mucous membranes.

H. C. L. LINDSAY, M.D., *Chairman*

SAUL S. ROBINSON, M.D., *Secretary*

May 13, 1941

Subacute Disseminated Lupus Erythematosus; Light-Sensitive Dermatitis.
Presented by DR. SAUL S. ROBINSON and DR. BEN A. NEWMAN.

S. B., a white woman aged *37*, has a recurring eruption on the face, ears, chest and upper extremities of four years' duration. Three days ago she was exposed to strong sunlight for one hour, and the eruption became more intense and spread to the backs of the hands. There are erythematous maculopapular and vesiculobullous lesions especially on the face, ears, forearms and backs of the hands. The blood and urine were normal. The treatment has consisted of weekly administration of bismuth subsalicylate (0.13 Gm.) intramuscularly.

DISCUSSION

DR. A. F. HALL: As this patient's lesions appear now I see nothing to convince me of the diagnosis of lupus erythematosus. She is definitely sensitive to light.

DR. WILLIAM GOECKERMAN: It is apparent that the patient's skin is sensitive to sunlight, but I believe that in spite of the dermatitis there are lesions on the ears with keratotic plugs which are characteristic of lupus erythematosus.

DR. SAMUEL AYRES: I think this case is one of lupus erythematosus with extreme photosensitivity. The patient has a tender abscessed molar tooth on the right side of the lower jaw. I strongly advise that this tooth be removed when the acute process has subsided.

DR. BEN A. NEWMAN: I have observed this patient's lesions for several months, and there is no question but that she has subacute lupus erythematosus. She has spots of erythema, scaling and typical plugging on the ears. Bismuth therapy was started several weeks ago, and the lesions showed decided improvement after several injections of a bismuth compound. The eruption is interesting from the standpoint of the bullae and vesicles, and these lesions are beginning to have a resemblance to lupus erythematosus. Of course, it is well known that lupus erythematosus is a light-sensitive disease. I should like to hear some comments about this type of vesicular reaction after exposure to sunlight. I wonder if such lesions have been seen before or whether this type of lesion may be a connecting link with lupus erythematosus of a bullous type that has been described.

DR. N. P. ANDERSON: Since there was a normal blood count, I cannot agree with the diagnosis of either acute or subacute disseminated lupus erythematosus. I think that this condition is a typical example of solar eczema or solar dermatitis.

DR. SAUL S. ROBINSON: This case is interesting because typical lesions of lupus erythematosus were present on the ears, face and backs of the hands when the patient first came for treatment. The lesions had been persistent for a number of months and responded readily to bismuth therapy. Last Sunday the

patient went out into the sun for one hour, and the next day the new acute lesions appeared. I do not believe that there is much question as to the presence of lupus erythematosus. The reported blood count was made at the time when the condition was quiescent. I did not make a blood count today when the patient was examined.

DR. KENDAL FROST: I believe that this woman has a solar dermatitis at present, and I also accept the diagnosis of lupus erythematosus. Whether or not lupus erythematosus may develop in the areas of dermatitis is a question which only time can tell. It is rather early after the exposure to the sun to make a diagnosis.

A Case for Diagnosis (Scleroderma? Alopecia Areata?). Presented by DR. JOHN D. RODGERS (by invitation).

M. F., a woman aged 38, about one year ago noted small hard spots in the skin after being on a reducing diet consisting of fruit juices and raw vegetables. After losing weight the patient noted hard areas in the skin that slowly enlarged. The physical examination reveals hard regions of induration, 2 to 6 cm. in diameter, in the deeper layers of the skin of the arm. There are two hard areas on the left arm and one on the right arm. There is no attachment of these areas to underlying tissues. There is no abnormal appearance of the overlying skin. The blood and urine were normal. There are four round well defined adherent areas on the scalp almost devoid of hair and associated with necrosis. The skin in these areas feels hard and inelastic. Atrophic areas are present on the arms and legs. The examination also reveals areas of induration under the skin in the region of the shoulders, thighs and axillas. The lesions in the axillas feel like hard glands.

Histologic examination of material from a scalp lesion on the scalp showed an irregular but thin and atrophic squamous layer of fairly dense stroma containing sweat glands, a few smooth muscles and several hair follicles. The basement layer of the epidermis was moderately pigmented, and there were some pigmented cells in the cutis. Deep in the cutis the collagen appeared in the form of large irregular bundles. The microscopic appearance seemed consistent with the diagnosis of scleroderma.

DISCUSSION

DR. WILLIAM GOECKERMAN: I should like to make a histologic examination of the node in the axilla. I do not think that this patient suffers from scleroderma; the lesions are definitely subcutaneous and evidently not in the skin. Too much subcutaneous atrophy remains when the lesions clear.

DR. BEN A. NEWMAN: I thought that the condition in this case fitted the condition that Weber has been describing as febrile nonsuppurative panniculitis.

DR. A. K. JENSEN: This woman's face was first examined by an orthopedic surgeon, who claimed that she was suffering from myositis.

DR. SAUL S. ROBINSON: I agree with Dr. Newman's diagnosis. I think that there are two conditions present. The patient has alopecia areata on the scalp and nonsuppurative panniculitis on the skin.

DR. H. C. L. LINDSAY: I think that there is alopecia areata on the scalp.

Xanthomatosis of the Tendons and Bones Associated with Disease of the Coronary Arteries. Presented by DR. BEN A. NEWMAN and DR. SAUL S. ROBINSON.

M. G., a man aged 47, had an attack of coronary thrombosis at the age of 40 and has since suffered from severe myocarditis. He was unaware of tendon nodules until six years ago, when he discovered large lesions in the achilles tendon. Numerous subcutaneous nodules have also appeared on the elbows, the tendons of the hands, around the ankles and on the tendons of the feet. The

patient has had alopecia areata of the scalp during the past two weeks. The blood and urine were normal. The electrocardiogram showed advanced myocardial damage with disease of the coronary arteries. Chemical examination of the blood showed cholesterol esters 268 mg., serum globulin 3.2 Gm. and uric acid 3.3 mg. per hundred cubic centimeters. Roentgenograms of the hands and feet showed destructive areas at the phalangeal articulations and metaphysial shaft. The histologic examination revealed typical xanthomatous deposits of cholesterol.

Xanthomatosis with Disease of the Coronary Arteries. Presented by DR. BEN A. NEWMAN.

N. B. O., a woman aged 49, first had nodules over the joints seventeen years ago. About ten years ago yellowish lesions appeared on both eyelids. The patient has been complaining of angina after severe exertion for the past year or two. The patient has two brothers with similar lesions. One brother had a coronary thrombosis in his early forties. The patient presents multiple firm subcutaneous nodules, varying in size from that of a pea to that of a plum on the elbows, surrounding the ankles, on the achilles tendon and along the tendons of the feet. Typical yellowish cutaneous xanthomatous plaques appear on the right elbow and on the eyelids. The blood and urine were normal. Chemical examination of the blood showed cholesterol 464 mg., serum albumin 4 Gm., serum globulin 1.8 Gm. and uric acid 2.8 mg. per hundred cubic centimeters. The electrocardiogram taken during anginal attacks was typical for a patient with disease of the coronary arteries.

DISCUSSION OF TWO CASES OF XANTHOMATOSIS WITH DISEASE OF THE CORONARY ARTERY

DR. WILLIAM GOECKERMAN: If I remember the 2 cases correctly, in one the condition was a classic example of the disease. In the other one the lesions seemed to me to be too soft and there was not enough yellowing of the skin.

DR. SAMUEL AYRES: It is interesting to observe these 2 cases of xanthoma with accompanying changes in the vascular system. I cannot think of any treatment of value other than restriction of intake of fat. I am wondering if any one has done any investigations with lipocaic. It is the only remedy that I can suggest, and I do not know how effective it would be.

DR. BEN A. NEWMAN: These patients are 2 of a group of 4 with associated disease of the coronary arteries and xanthomatosis. The 2 other patients failed to appear. I hope to have a symposium on this group. I think that these cases illustrate certain factors that have been mentioned in the literature, particularly during the past four years.

A Case for Diagnosis (Contact Dermatitis?). Presented by DR. H. C. L. LINDSAY.

J. W. H., a man aged 26, states that two months ago the skin on his hands became dry and split over the dorsa of the distal finger joints. The left ear became scaly at the external meatus, and the scaliness extended to the lower half of the ear. The left upper eyelid also became inflamed and scaly. Scaling on both elbows has been present off and on for a considerable length of time. The lesions are sharply demarcated on the thumbs with involvement of the area around the nails. There is redness on the fingers that is practically limited to the tips and extends back as far as the distal joints. The patient handles carbon paper, but patch tests with carbon paper gave negative reactions. Red papules are scattered over the left side of the face, especially in the area where the patient rests a telephone receiver during his work. The patch of dermatitis on the left thumb is a scaling, rectangular, thickened, inflamed area which is sharply demarcated. The lesions on the hands are not pruritic, but those on the eye, ear and cheek itch intensely.

DISCUSSION

DR. WILLIAM GOECKERMAN: I should search carefully for a cause of contact dermatitis.

DR. KENDAL FROST: Symmetric dermatitis affecting the hands and sometimes partly the face and neck is simply an eczema, and I also think that there is a possibility that the condition in this case is contact dermatitis or multiform erythema.

DR. SAUL S. ROBINSON: I have seen a few patients with this condition, and they are all interesting from a diagnostic standpoint. Many of them have been tested for contact dermatitis without any cause being found. In this case the lesions on the lower eyelids, the side of the face, the ears, the hands and the fingers suggest neurodermatitis. I think that all contact irritants should be ruled out, and if the condition still persists treatment for neurodermatitis should be instituted.

DR. H. C. L. LINDSAY: I am inclined to agree with Dr. Goeckerman. There are 2 other persons in the patient's place of employment, and they handle a large amount of carbon paper. Although this patient has been tested for twenty-four hours with this carbon paper, he has had no reaction to the patch test. He thought that the handling of carbon paper every day was irritating the tips of his fingers, but the inconsistent part of this logic is that he is right handed and that most of the eruption is on the ear and on the left hand. I thought that the patient might be suffering from a fungous infection on the hand and that the eruption on the face was transferred from his hand.

DR. A. F. HALL: Although I have never seen a dermatitis from nail polish occurring on the backs of the fingers, I should be interested to find out if this patient uses nail lacquer, because the eruption on the eyelids and in other parts fits in with the dermatitis caused by nail lacquer irritation.

CLEVELAND DERMATOLOGICAL SOCIETY

H. N. COLE, M.D., *President*

C. G. LAROCCO, M.D., *Secretary*

JAMES R. DRIVER, M.D., *Reporter*

Feb. 27, 1941

Chronic Ulcerative Radiodermatitis (Encouraging Results Following Treatment with Aloe Vera Leaf and Aloe Vera Ointment). Presented by DR. HAL ELSON FREEMAN and DR. JAMES E. ENGELER.

M. W., a white housewife aged 54, presented from the department of dermatology and syphilology, Cleveland City Hospital, first noticed a retraction of the left nipple in July 1939 and a "lump" in the left breast in January 1940. A radical amputation of the breast with dissection of the axillary lymph nodes was performed. Histologic examination revealed an undifferentiated adenocarcinoma High voltage roentgen radiation in divided doses for a total of 3,200 r was administered to the axilla and breast.

The reaction on the skin was followed in about six weeks by a progressively chronic ulceration. This was treated with boric acid ointment, débridement, diluted solution of sodium hypochlorite U. S. P., acriflavine, azochloramid, etc. The

response was slight and slow. After nine months the patient was transferred to the dermatologic service, on Jan. 15, 1941.

Examination reveals an area of discoloration and telangiectasia involving the left breast and an area of deep ulceration about 10 cm. in diameter on the upper portion of the left breast and in the left anterior axillary fold.

Treatment consisted of the application of 30 per cent ointment of Aloe vera twice weekly following débridement. The improvement has been greater in five weeks with this therapy than it was in the previous nine months. The ulceration in the left anterior axillary fold has healed, and that over the breast is filling in rapidly.

A Case for Diagnosis (Post-Traumatic Neuromyelopathy with Trophic Ulceration? Dermatitis Factitia?). Presented by DR. HAL ELSON FREEMAN and DR. E. B. HEISEL.

M. C., a white woman aged 46, presented from the department of dermatology and syphilology, Cleveland City Hospital, complains of numbness and sores on both buttocks.

In October 1938 she fell through a railing of a second story porch while dusting a rug. At that time she fractured her spine at the level of the second lumbar vertebra. After this accident she lost control of the urethral and anal sphincters. Superficial sensation of the saddle area on the perineum and the buttocks was also lost. Several oval, dollar-sized areas of ulceration appeared on the buttocks four days ago.

The deep reflexes are present and physiologic. There are a tender scar in the lumbar region at the site of the old injury, loss of sensation over the buttocks and perineum and loss of epicritic sensibility down as far as the knees. There are several oblong or ovoid superficial, denuded, slightly inflamed lesions on both buttocks. These are all arranged longitudinally to the long axis of the body. Urinary and fecal incontinence is present.

Serologic tests for syphilis gave negative results. Roentgenograms showed an old fracture of the second lumbar vertebra. Iodized poppyseed oil injected into the cistern showed no definite evidence of compression of the spinal cord.

DISCUSSION

DR. R. E. BARNEY: I think the condition in this case is a classic example of factitial dermatitis. I noted what seemed to be a trickle extending down from one of the lesions that I thought was due to some escharotic that had been applied. The lesions, furthermore, have a suggestive necrotic appearance, such as could be produced by phenol. The fact that they appeared in only four days is suggestive of a self-inflicted lesion.

DR. H. J. PARKHURST, Toledo, Ohio: The patient's history of post-traumatic anesthesia, together with the appearance and distribution of these lesions, was more in favor of a diagnosis of burns due to contact with a hot radiator. Burns on areas of anesthesia such as this are not uncommon.

DR. J. E. RAUSCHKOLB: I saw a patient several years ago with similar burns on the buttocks caused by sitting on a hot steam radiator. The areas involved were the size and shape of the radiator sections.

DR. HAL ELSON FREEMAN: I, too, thought of this possibility when I first saw this patient. She insists, however, that she did not sit on a radiator and does not have such radiators in her home.

DR. E. W. NETHERTON: I think that if this woman intentionally produced these lesions, she is an artist. They are symmetric. I think they are trophic ulcers in an area of anesthesia with some type of trauma responsible for it. If they were caused by chemicals, how would one explain the method of application?

DR. HUGO HECHT (by invitation): It is possible to find out with chemical examination whether the lesions are atrophic or due to chemical burns. I think that in this case they are burns due to contact with a radiator. It would be impossible for the patient to apply a chemical in such symmetric fashion in this area. She would have had to have an accomplice. If this were true, it would have been done with the idea of collecting insurance or with some other motive, such as a desire for sympathy.

DR. B. F. BARNEY, Columbus, Ohio: The point has been raised that it would be next to impossible for this woman to have produced these lesions herself by the application of some chemical. In my experience most of these patients are very ingenious. She might have stood before a mirror and placed cotton pledgets saturated in acid on the areas. The lesions do not show any particular artistic ability. I think it would be easy to touch these areas.

DR. R. E. BARNEY: She could take a heavy piece of paper and cut out the design of these lesions, place material saturated with acid beneath the paper and sit on it.

DR. J. R. DRIVER: I took the trouble to measure the sections of the radiator in this room, and the five lesions on her buttocks correspond exactly to five sections of the radiator. It seems entirely logical that, although she does not recall the incident, she did sit on a radiator and thus received this injury.

Tertiary Syphilis with Obstruction of the Azygos and Hemiazygos Veins by an Aneurysm. Presented by DR. HAL ELSON FREEMAN and DR. U. G. MASON (by invitation).

F. S., a white man aged 52, presented from the department of dermatology and syphilology, Cleveland City Hospital, had a penile chancre in 1919. He sought medical advice in October 1940 because of night sweats and pain in the left interscapular region.

A reading for blood pressure was not obtainable for the right arm, and for the left the reading was 100 mm. of mercury systolic and 76 mm. diastolic. A tracheal tug is palpable. There is a beltlike distribution of dilated superficial veins about the lower part of the chest. The mediastinum is enlarged, especially to the right, and the heart is enlarged to the right and to the axillary line on the left. A loud diastolic murmur is heard over the aortic area. The reflexes are present and hyperactive. The hemogram and the urine were normal. The Kline, Eagle and Wassermann reactions of the blood were strongly positive. The spinal fluid showed an increase in globulin, 50 cells per cubic millimeter, a strongly positive Wassermann reaction and a gum mastic curve reading of 5544444443. Fluoroscopic and roentgenographic studies of the heart and aorta showed only slight enlargement of the heart and an aneurysmal dilatation of the entire aorta with a localized saccular dilatation above, to the left and posteriorly.

DISCUSSION

DR. H. H. JOHNSON: In addition I noted that the patient seemed to have a good deal of venous dilatation on the right upper part of the thorax, probably due to obstruction of the subclavian or innominate vein.

DR. HAL ELSON FREEMAN: I think what Dr. Johnson says is true; the man has a saccular aneurysm which could cause an obstruction of the large veins in the mediastinum.

Orthostatic Hypotension in a Case of Tertiary Syphilis. Presented by DR. HAL ELSON FREEMAN and DR. JAMES E. ROBERTSON (by invitation).

S. V., a white man aged 42, presented from the departments of dermatology and syphilology and of medicine, Cleveland City Hospital, came to the hospital in

December 1940 because of pain in the upper part of the abdomen for one year and vomiting of two weeks' duration. The abdominal pain was more severe about thirty minutes after meals. He had received a small amount of treatment for syphilis in 1933. In addition to vomiting, the patient recently observed that he became faint when he suddenly assumed the upright position. This was first observed when fluoroscopic examination of the stomach had to be postponed because the patient could not stand upright for the examination. It was again noticed when the patient grew faint and weak and had to lie down when he tried to sit up in bed to use the bedpan.

The pupils are fixed to light and in accommodation, and there is diminished vibratory sensation in the lower extremities. The deep reflexes were physiologic. The blood pressure varied between 115 and 125 mm. of mercury systolic and 70 to 75 mm. diastolic when the patient was recumbent. One minute after assuming the sitting position the values became 55 to 60 mm. systolic and 40 mm. diastolic. After the change of position and the fall in blood pressure, the heart rate became slow and the heart beats irregular.

The hemogram showed a mild degree of secondary anemia. The icteric index showed 7 units of bilirubin. Other chemical determinations of the blood and the urine were normal. The Wassermann reaction of the blood was weakly positive, and the Kline reaction was strongly positive. The spinal fluid showed 60 cells per cubic millimeter in December 1940 and 20 cells in January 1941. Increased globulin was present. The gum mastic curve reading was 4332110000, and the Wassermann reaction of the spinal fluid was strongly positive. Roentgenograms of the gallbladder, stomach and duodenum showed no pathologic evidence.

Therapy has consisted of twelve intramuscular injections of iodobismitol with saligenin three times weekly.

DISCUSSION

DR. H. G. MISKJIAN: Has Dr. R. W. Scott, the cardiologist of the Cleveland City Hospital, observed this case, and, if so, what does he think of it?

DR. HAL ELSON FREEMAN: There have been a few cases of orthostatic hypotension described by Dr. G. S. Baker (*Proc. Staff Meet., Mayo Clin.* **13**:162, 1938). He stated the belief that this condition is always caused by lesions in the central nervous system. Our patient has tabes dorsalis. This was true also of the patients described by Dr. Baker.

DR. JAMES E. ROBERTSON (by invitation): Dr. Scott seemed to think the condition was due principally to involvement of the splanchnic sympathetic nervous system, so that there was characteristic rapid dilation of the vessels causing drainage of blood to this area. Our patient is being treated with a head-up position recommended by Dr. Baker, and he has shown some improvement.

DR. HAL ELSON FREEMAN: I should like to have the opinion of any of the members as to the advisability of using malarial treatment on this patient.

DR. J. R. DRIVER: I believe that malarial treatment is contraindicated because of the hypotension. However, I think that cautious use of another form of fever therapy, such as foreign protein, could be tried to see how he stands it.

DR. H. N. COLE: I think that bismuth therapy should be continued for some time before any other form of treatment is considered.

Otomycosis. Presented by DR. HAL ELSON FREEMAN and DR. JAMES E. ENGELER.

E. W., a student nurse aged 21, presented from the department of dermatology and syphilology, Cleveland City Hospital, has had a dry scaling, moderately pruritic eruption in her external ear canals for the past four years. Seborrheic dermatitis and also psoriasis have been considered in the past as possible diagnoses.

Scrapings from the external auditory canals taken Oct. 26, 1940 were placed on Saboraud's sugar-proof medium. After three weeks a 1.5 by 1.5 cm., buff and cream-colored, convoluted pure fungous growth was available for study. This culture has been transplanted and carried through three subculturings. These subcultures present a brown, irregular and convoluted appearance. A culture mount showed numerous interlacing segmented hyphae. The fungus has been tentatively identified as Trichophyton topicale.

DISCUSSION

DR. J. A. GAMMEL: I believe this fungus is pathologic. It is often difficult to classify growths of this type, and from the culture presented I am not sure just what it is. I suggest further cultural studies. It is one of the more uncommon species.

Tertiary Syphilis; Pseudoepitheliomatous Hyperplasia in a Gumma of the Tongue; Pulmonary Tuberculosis. Presented by DR. HAL ELSON FREEMAN and DR. E. B. HEISEL.

W. D., a white man aged 46, presented from the department of dermatology and syphilology, Cleveland City Hospital, noticed a sore on the right side of his tongue in April 1940. It has progressed and has destroyed most of the tongue. He states that his tongue was always large and that he has used various types of trauma in an effort to reduce its size. He has known for many years that he had syphilis but has never received any treatment for it.

The anterior two thirds of the tongue is absent, and the stump of the tongue and the floor of the mouth are ulcerated and in areas covered by verrucoid hyperplasia. Several teeth are missing, and the others are dirty and in poor repair. The submaxillary lymph nodes are palpable and firm bilaterally but are small and probably not abnormal. Distant breath sounds are heard at the apex of the left lung, and the percussion note is dull.

Serologic tests for syphilis gave positive reactions. A roentgenogram of the skull showed a large sella turcica. A roentgenogram of the chest showed a soft infiltration in the upper third of both pulmonary fields and a cavity 3 cm. in diameter in the right subapical region.

Histologic examination of a specimen from the destructive lesion of the tongue showed an extreme degree of branching acanthosis. There was an extensive subpapillary leukocytic infiltrate which was primarily lymphocytic. Numerous plasma cells were seen throughout the section, and the infiltrate was practically purely composed of plasma cells in the deeper part of the corium. Neither tubercles nor giant cells were seen. The hyperplastic and metaplastic squamous cells which were evident did not display the mitotic figures and other evidences which characterize a true squamous cell carcinoma.

DISCUSSION

DR. EUGENE ARDAY, Lakewood, Ohio: I take exception to the diagnosis of a nonmalignant disease of the tongue. I am sure that I saw nests of epithelial cells in the corium of the section that I examined. Clinically and histologically the condition is carcinoma of the tongue.

DR. HAL ELSON FREEMAN: On careful study of the sections, I was unable to find any evidence of carcinoma. There were no mitoses present, and I could not demonstrate any epithelial cells in the corium. In such an extensive disease as this, one would expect to find obvious metastases by this time if the lesion were carcinomatous.

Poikiloderma Atrophicans Vasculare (Jacobi). Infectious Eczematoid Dermatitis. Presented by DR. E. B. HEISEL and DR. HAL ELSON FREEMAN.

C. L., a white man aged 56, presented from the department of dermatology and syphilology, Cleveland City Hospital, for the past twenty-five years has had on the forearms and ankles asymptomatic "white spots" appearing on deeply colored red skin. He has worked as a fireman for thirty-five years.

On the flexor surfaces of the forearms and around the ankles there is a poorly delimited reticulum of deeply colored red skin of normal texture. In the interstices there are areas of depigmented and atrophic skin varying in size and shape. There are telangiectases on the dorsa of the feet and in the deeply colored reticulum.

Serologic tests for syphilis gave negative results. Histologic examination of a section revealed a moderate degree of hyperkeratosis. The epidermis revealed areas of atrophy and intercellular and extracellular edema. The upper third of the cutis was the seat of a sharply delimited, loosely arranged infiltrate. In some areas the basal layer was broken through by this infiltrate from the cutis. It consisted mainly of lymphocytes, a few mast cells, numerous eosinophils and scattered collections of pigment. Numerous collagen fibers showed fragmentation and basophilic degeneration. Special connective tissue stains (Weigert) showed considerable fragmentation of the connective tissue in half of the corium.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: I disagree with the diagnosis. This man has been a fireman, firing a boiler, for about thirty-five years, and for about twenty-five years he has had this atrophic, mottled condition on the forearms and less pronounced on the legs. I feel that the condition is erythema ab igne due to years of exposure to heat.

DR. E. W. NETHERTON: The amount of atrophy present is not as great as one would expect in a case of poikiloderma atrophicans vasculare. I favor a diagnosis of parapsoriasis.

DR. GEORGE W. BINKLEY: The histologic picture in this case is consistent with a diagnosis of parapsoriasis variegata.

DR. HAL ELSON FREEMAN: At first I thought the condition was parapsoriasis clinically, but I did not think the appearance of the histologic section was consistent with the diagnosis.

Keratosis Blennorrhagica. Presented by DR. E. B. HEISEL and DR. HAL ELSON FREEMAN.

M. P., a white man aged 30, presented from the department of dermatology and syphilology, Cleveland City Hospital, complains of a sore on the penis and of a painful left great toe, heel and ankle of two months' duration. He gives a history of a penile discharge three months ago and of painful testes two months ago, both of which have receded under therapy. There is a history of having had gonorrhea in 1921, 1936 and 1937 and Malta fever in Spain in 1937.

There is a symmetric eruption on the lateral portions of the soles consisting of round, conical hyperkeratotic nodules, some of which are covered with thick dry scales. The left great toe is tender, red, swollen and warm. Around the entire corona and coronal sulcus there is a sharply delimited, reddened keratotic process which is covered with dry, dark brown crusts.

The hemogram showed a moderate leukocytosis with a relative and absolute polymorphonuclear leukocytosis. The urine was normal. The reaction to a complement fixation test for gonorrhea was weakly positive. Serologic tests for syphilis gave negative results. Determinations of uric acid in the blood revealed 4.4 mg. per hundred cubic centimeters on one occasion and 3.5 mg. on another. A Gram stain of a prostatic smear showed only many leukocytes and no gonococci. A Gram stain of a smear from pustules on the inner part of the thighs auto-

inoculated from the soles revealed gram-negative, coffee bean–shaped extracellular diplococci but no intracellular organisms. Roentgenograms of the left great toe and ankle were normal.

Histologic examination of a section taken from a keratotic nodule on the soles revealed an extreme degree of hyperkeratosis and parakeratosis and a moderate degree of acanthosis and spongiosis. Scattered collections of small round cells and a few erythrocytes and a few leukocytes were also noted. In the corium there was a small, round cell infiltrate distributed mainly perivascularly. Gram stains of a similar section revealed no gonococci.

Therapy consisted of 68 Gm. of sulfanilamide given orally, eight paroxysms of chilling and fever produced by the intravenous injection of killed typhoid-paratyphoid A and B organisms and a five hour treatment in the Kettering hypertherm.

DISCUSSION

DR. H. N. COLE: Therapy has largely altered the characteristic appearance which this man presented when he entered the hospital. In spite of the fact that the organisms are not entirely characteristic in the stained smears, I believe this condition is a typical clinical example of keratosis blennorrhagica.

Avitaminosis (Pellagra and Cheilitis). Presented by DR. JAMES E. ENGELER and DR. HAL ELSON FREEMAN.

I. W., an emaciated white man aged 70, presented from the department of dermatology and syphilology, Cleveland City Hospital, complains of weakness, sore mouth and an eruption on the face, hands and feet. For several weeks his diet has consisted chiefly of bread and black coffee. He states that his memory has recently been failing him.

The skin on the forehead, on the bridge of the nose and in the nasolabial folds is thickened and covered with pinpoint-sized keratoses, which give the skin a nutmeg grater feel. On the dorsa of the hands and extending to the wrists, where it is sharply delimited, there is a bullous, erythematous, scaling and fissured dermatitis. On the extensor surfaces of the elbows and on the back of the neck there are circumscribed erythematous and scaly patches. On the perineum and inner aspects of the thighs there is a butterfly-shaped area of scaly dermatitis showing hyperpigmentation. There is edema of both ankles with hyperpigmentation of the skin on the dorsa of the feet.

The hemogram showed 50 per cent hemoglobin and 3,740,000 erythrocytes and 5,250 leukocytes per cubic millimeter, with 90 per cent polymorphonuclear leukocytes and 10 per cent lymphocytes.

Syringoma. Presented by DR. JOSEPH H. SHEPARD, Columbus, Ohio.

O. B., a white woman aged 58, states that at the age of 17 she first noticed some small growths on her face. At the age of 24 she noticed a similar lesion on the scalp. Since then there has been a gradual development of numerous tumors on the scalp. Their growth has been slow, each gradually enlarging, until almost the entire scalp has become involved. Her father, who died at the age of 44, was said to have had several lesions on the scalp resembling those of the patient. A brother who died at the age of 43 also had some tumors on his scalp. A sister who died in childhood had no similar lesions.

The scalp is covered with tumors varying in size from a fraction of a centimeter to 5 cm. across, and some are raised 2.5 cm. above the surface of the skin. They are smooth and rounded, some lobulated, and vary from skin color to a definite rosy or violaceous color.

The lesions on the face are pinhead sized to split pea sized, smooth and firm to the touch, and all are the color of normal skin or slightly lighter. They are on the forehead, on the eyebrows, between the eyebrows, on the sides of the nose, around the mouth and on the cheeks near the nose.

Serologic tests for syphilis gave negative results. The hemogram was normal.

The microscopic features of sections from the scalp and from the eyebrow were essentially the same. The cells making up the tumor stained rather deeply and were grouped together in round or oval clumps surrounded by bands of connective tissue in which some hyaline degeneration had taken place. The tumor mass was separated from the thin flattened epithelium by a narrow band of normal tissue. The cells were round or cylindric, had large nuclei and were definitely basal cells.

DISCUSSION

DR. GEORGE W. BINKLEY: This woman's history shows the familial characteristics of this disease. The tomato-like tumors are typical of cylindroma.

The symmetric lesions on the forehead and face, in front of the ears and also on the upper lip and chin might well be considered to be lesions of epithelioma

A, "turban tumors" (cylindroma); *B*, multiple benign epitheliomas.

adenoides cysticum on the basis of their difference in color and, also, because a few of them show dark blue-black discoloration in the depth of the tumor, which is supposed to be characteristic of epithelioma adenoides cysticum.

Anatomically, both of the sections were characteristic of cylindroma. They did not show the dilated sweat glands which are the factors of syringoma.

MANHATTAN DERMATOLOGIC SOCIETY

J. FRANK FRASER, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

March 11, 1941

A Case for Diagnosis (Neurotic Excoriations with Pigmentation? Urticaria Pigmentosa?). Presented by DR. E. WILLIAM ABRAMOWITZ.

Miss E. B., a private patient aged 22, presents pea-sized areas of pigmentation all over the trunk. The eruption has been appearing for the past eleven years and was first accompanied by itching, but this has been absent for the past few years.

When she was first seen on Jan. 17, 1941 she presented small red papular lesions with central bleeding points and crusts. These left pigmentary stains with a central depigmentation.

The patient admitted picking these lesions when they first started to appear, but she has not done this in the past few years. She is of a nervous temperament and has been rubbing herself vigorously with a towel after bathing. Since she stopped this practice the new lesions are fewer and the pigmentation is less noticeable.

Her menstrual periods were irregular a few years ago, and she received injections of some estrogenic substance, with improvement.

Microscopic examination showed a picture in part similar to that of neurodermatitis. Only an occasional mast cell was present, not sufficient to warrant designating the condition as urticaria pigmentosa.

DISCUSSION

DR. HOWARD FOX: This condition looks to me like the type of urticaria pigmentosa seen in adults, though it is a little puzzling that the lesions did not become urticarial on friction. The lesions are all reddish and uniform in size, smaller than a split pea, as is usual in this type of disease.

DR. HERMAN SHARLIT: Did any one entertain the idea that this condition might be healed acne with pigmentation?

DR. SAMUEL PECK: I think the question of atrophy was ruled out because of the uniformity and the distribution of the lesions. The eruption seemed to extend far down along the sides of the chest and the rest of the trunk, and I think that histologically one would expect to find typical structures if the proper biopsy specimen was taken. I should expect to see a typical histologic structure. I still think one could possibly make the diagnosis of urticaria pigmentosa.

DR. WILBERT SACHS: I think healed acne can be ruled out, because there is an active process in the cutis. I do not believe the diagnosis is urticaria pigmentosa, because I especially studied the slides with this in mind. There was a neurodermatitis reaction. Even without mast cells one does not find this type of reaction. Certainly, if the condition were urticaria pigmentosa one would expect to find many more mast cells. An occasional mast cell is found in any inflammatory process.

DR. J. FRANK FRASER: I think it was Hartzell who first pointed out that mast cells might not show in one stage of the development of an individual lesion but might show in a later stage. I think it is frequently necessary to perform more than one biopsy in a case of this kind. Wise's experience corroborates this view, and I might also say that while working on this subject I sometimes was obliged to make as many as five or six histologic examinations before deciding that the condition was actually urticaria pigmentosa. For these reasons I advise that other sections be taken from different lesions and examined again, because there is still the possibility, notwithstanding the fact that the present sections do not show any mast cells, that this case may be one of urticaria pigmentosa.

DR. E. WILLIAM ABRAMOWITZ: The feature of this eruption was the pigmentation. I also considered the possibility of dermatitis herpetiformis in this case, because there was grouping in certain areas. She does not complain of itching now.

Lichen Striatus. Presented by DR. GEORGE M. LEWIS.

A. G., a girl aged 13, was first seen at the New York Hospital on April 26, 1940. She had first noticed an eruption on her left arm three months before. There had been gradual extension of the condition but no evidence of involvement of other parts of the body. The diagnosis of lichen planus was considered,

but no definite papules were observed and no lesions were present in the mouth. The lesions were lichenified, discrete, confluent, scaly and grouped in linear formation. The possibilities of nevus or of verruca plana were also suggested. The eruption gradually faded, and when she was seen in February 1941 only a few flat papules were present, suggestive of flat warts.

Histologic examination revealed acanthosis and hyperkeratosis. There was an inflammatory reaction consisting of lymphocytes, plasma cells and occasional polymorphonuclear leukocytes mainly in the region of the hair follicles but also extending between the rete cones and in small linear projections in the corium near the hair follicles. The Wassermann reaction was negative.

DISCUSSION

DR. WILBERT SACHS: Clinically, there were a few small papules not unlike those seen in lichen nitidus. Microscopically, there was a lichen nitidus reaction in the cutis, but there was something much more than that not observed in lichen nitidus. There was a definite infiltration around the adnexa. There were also some histiocytes. The superficial portion would go well with lichen nitidus but not this deep infiltration. I do not know what diagnosis to make. The condition is not a nevus, and it is more than just a dermatitis. I could not say whether or not it is a tuberculid.

DR. DAVID BLOOM: I think the condition in this case is dermatitis linearis. In the period of involution the papules may resemble lichen nitidus.

DR. GEORGE M. MACKEE: I did not see the patient, but I saw the photographs, which show papules of a color different from that of the normal skin. They are arranged in a linear manner, and the condition looks like lichen planus linearis.

DR. HOWARD FOX: Dr. Senear recently reported a group of cases of a condition he called lichen striatus. In most of these it resembled either linear lichen planus or linear nevus. However, because in all of them it cleared up within a few months, nevus could be ruled out. The comparatively rapid course would also be against the diagnosis of lichen planus.

DR. HERMAN SHARLIT: Could not a tuberculid be considered?

DR. GEORGE M. LEWIS: The diagnosis of linear lichen planus was considered. Some of the lesions were discrete and others confluent; some were flat topped. There were no umbilicated lesions. The distribution was in a linear form. There was practically no pruritus, and no lesions were seen on the mucous membranes or on other parts of the body. In Senear's series the patients were young girls and the lesions were all unilateral and on an upper extremity. The histologic appearance fits in with the diagnosis. Nevus, verruca plana and lichen nitidus could be ruled out on clinical and histologic grounds.

Darier's Disease. Presented by DR. MAX SCHEER for DR. PAUL BECHET.

W. S., a youth aged 18, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 4, 1941, with a generalized eruption that had been present since infancy. The family and personal histories were irrelevant. His general health is good.

The eruption first appeared on the face at 1½ years of age, then on the trunk and inner surfaces of the legs and last on the dorsal surfaces of the hands. It came on slowly, involving all the areas at the age of 14. A year ago, when he was in a CCC camp for six months in Oregon and much exposed to the sun, the lesions on the face, chest and back retrogressed considerably. Many of the patches on the chest seemed to have cleared, but they reappeared when he returned to New Jersey in September 1940. With this exception, there never seemed to be any change in the eruption. There is a slight itching of the back in the summer.

The patient is a well developed youth, about 5 feet 6 inches (168 cm.) in height, weighing 160 pounds (72.5 Kg.) and appearing to be in perfect health. The eruption is symmetric, located on the entire face (except on the upper and lower eyelids), conchae of the ears, trunk, axillas, loins, groins, inner surface of the legs, middle of the dorsal surfaces of the feet and dorsal surfaces of the hands. The eruption is profuse, dull erythematous and rough looking, even at a distance of several feet. On close inspection it is seen to consist of fine pinpoint-sized to pinhead-sized rough-topped papules, so closely set as to appear to be in continuous patches, with some small, irregular, normal-appearing areas between. Many have follicular plugs, most numerous on the sides of the neck and imparting more of a grayish tinge. The papules are verrucous-like in the retroauricular areas and larger on the chest, where they are distributed in a V-shaped manner, and in the scapular regions. There are only occasional papules on the abdomen and lower parts of the back. The lesions are both perifollicular and follicular, the papules being pierced by hairs and easily demonstrable on the inner surface of the thighs. On the dorsal surfaces of the hands there are distinct discrete flat-topped match head–sized to hemp seed–sized papules, not scaly and resembling flat warts. On diascopic pressure the erythematous diffuse areas are easily compressible, disclosing white slightly scaly areas. There are also lesions on the soft palate and the dorsal surface of the tongue. The nails are free.

The results of routine laboratory tests were normal. The histologic section taken from the back and examined by Drs. Satenstein and Sachs revealed the typical structure of Darier's disease: "At one part of the epidermis there is considerable acanthosis. The surface is verrucous and covered by a densely laminated horny layer, which extends down deep into the epidermis. The basal layer appears to be intact, and directly above it is a space in which there are small round hyalinized dyskeratotic cells—*corps ronds*. There are a moderate dilatation of vessels and a sparse small round cell infiltration in the upper part of the cutis."

DISCUSSION

Dr. Max Scheer: There is no special point about this case except that we hope to present the patient again six months or a year from now after vitamin A therapy.

Monilethrix. Koilonychia. Presented by Dr. George M. Lewis.

G. G., a girl aged 16, is presented from the New York Hospital. She has had trouble with her scalp and nails all her life. The hair fails to grow out to an appreciable length except during the summer months, when it may reach down to the shoulders. At other times the hair is short, and using a comb removes much of it.

The top of the scalp has the appearance of being closely cropped, but with no evidence of actual alopecia. In the frontal and parietal regions the hair is longer. On manipulating the scalp breaking of hair occurs. No beading or nodes can be detected, even with the aid of a hand lens. The surface of the scalp is normal except for an associated keratosis pilaris on the back of the scalp and neck. No other hairy parts are similarly affected. All the finger nails are dystrophic and show the spoon nail appearance. The toe nails are unaffected. No other epidermal changes can be detected.

The Wassermann reaction was negative. After a search, hairs were found which showed the typical undulating appearance of monilethrix.

DISCUSSION

Dr. George M. MacKee: I agree with the diagnosis. The fact that the condition is congenital plus the concomitant keratosis pilaris, the presence of short brittle hairs, many of which have broken off, and the dry, strawlike quality of the hair are in favor of the diagnosis, in spite of the fact that I could not see any nodes with the unaided eye. However, I did see a hair under the microscope which showed some undulation, which is so characteristic of monilethrix.

DR. E. WILLIAM ABRAMOWITZ: At a meeting of the Brooklyn Dermatological Society (ARCH. DERMAT. & SYPH. **21**:1054 [June] 1930) a report was made of a patient with monilethrix. She had epilation of the scalp with roentgen rays, and after that the hair reappeared apparently normal. In a few months the beaded hairs reappeared. The roentgen ray epilation was later repeated with similar results. The question came up as to how many times this could be continued with safety. I consider such treatment dangerous.

DR. WILBERT SACHS: There now are 2 definite cases of this disease at the New York Post-Graduate Medical School and Hospital, and because of the associated keratosis pilaris my brother (Dr. Perry M. Sachs) is going to try high doses of vitamin A. I wonder if any one has any experience with vitamin A in the treatment of this particular disease.

DR. HOWARD FOX: Has anybody ever seen a cure or even appreciable improvement in cases of this kind?

DR. E. WILLIAM ABRAMOWITZ: In reference to Dr. Fox's question, many years ago Dr. Satenstein treated the follicles containing the beaded hairs with electrolysis; while the hairs failed to reappear, the follicles remained keratotic. Thallium acetate was tried in the treatment of monilethrix with the same result; epilation was obtained, and then the condition recurred.

DR. ANTHONY C. CIPOLLARO: Spoon nails occur in association with so many different diseases and under varying environmental states, especially in persons whose occupation requires them to use alkaline solutions, especially soap. So far as I know, monilethrix and koilonychia have never been reported as occurring in the same person. My feeling is that the changes in the nails which this girl presents are probably part of the same congenital process that accounts for the changes in the hair.

DR. GEORGE M. MACKEE: There are probably a number of persons with potential congenital koilonychia which never becomes manifest unless the hands are immersed for fairly long periods in alkaline solutions; then koilonychia is apt to develop. In all my cases of monilethrix there was no koilonychia. It would have been interesting—and would be interesting in other cases of monilethrix—to try immersing the fingers in an alkaline solution for one-half hour a day for several weeks to see if koilonychia would develop. The hair grows normally for a short time and abnormally for a time. Sometimes the hair may grow normally for weeks or months.

DR. GEORGE M. LEWIS: The association of monilethrix and koilonychia in the same patient is unique in my experience.

A Case for Diagnosis (Atrophic and Pigmented Patches; Convulsions and Hemorrhage from the Stomach and Intestines). Presented by DR. HOWARD FOX.

W. S., aged 23, a native-born American, a merchant seaman, was referred from the Ellis Island Hospital, through the courtesy of Dr. A. R. Sweeney. He had been sent from the Stapleton Hospital for neuropsychiatric examination on account of recurring convulsive attacks. An eruption was first noticed about two years ago, its onset coinciding approximately with the convulsive attacks. The eruption was generalized and mainly confined to the trunk, including the anterior, posterior and lateral aspects. It consisted of ill defined superficial areas varying in size from that of a small coin to that of the palm. All showed varying degrees of pigmentation, being pronounced in only a few areas. The color was light yellowish brown. Many of the patches were distinctly atrophic when viewed at the proper angle. A few had a stippled appearance in the central parts due to small pinhead–sized discrete points of lighter color than the intervening parts of the patch. There was no appreciable infiltration and no scaling or objective evidence of itching. The lesions presented no subjective symptoms, and no abnormal sensation was noted by the prick of a pin. The patches were asymmetric and showed no special grouping.

The chief complaint consisted of sudden attacks of unconsciousness, which had occurred at intervals of six months. They occurred in the evening and were preceded in the morning by gastric distress and headaches. During the attacks, which lasted about fifteen minutes, the patient was unconscious with rigidity of the muscles but without convulsion. The tongue was bitten, but there was no frothing at the mouth. The attacks were followed by vomiting of blood and for the next three days by passage of tarry stools.

Examination of the blood showed a normal hemoglobin content and a normal number of red and white cells. The differential ratio showed a moderate lymphocytosis, with 51 per cent polymorphonuclear leukocytes, 43 per cent lymphocytes, 2 per cent transitional forms and 4 per cent eosinophils. The bleeding time was six minutes, and the clotting time four minutes. The Wassermann and Kahn reactions of the blood were negative. Chemical examination of the blood gave normal figures for nonprotein nitrogen, urea and chlorides. The urine and the results of a sugar tolerance test were normal. Roentgenograms of the skull and of the chest showed no abnormalities.

The family and personal history gave no relevant information. The patient was of medium size, well nourished and healthy in appearance.

DISCUSSION

DR. A. R. SWEENEY (by invitation): I do not have much to say in regard to the cutaneous condition. The patient has not yet been completely studied to see what relation, if any, exists between the cutaneous condition and any possible neurologic condition. A biopsy has just been made, but I have no report as yet.

DR. SAMUEL PECK: I am just wondering whether the pigment is due to melanin or to blood. There is a history of hemorrhage, and the areas look as though they have pinhead-sized atrophic spots in an area of pigmentation, compared to the normal skin. The histologic examination will tell, but I wonder if blood pigment could be ruled out on clinical grounds.

DR. A. R. SWEENEY: Perhaps the patient bit his tongue and the blood came from that source. He may have swallowed the blood, and part of it may have been vomited and part may have gone into the intestinal tract. No studies have as yet been done.

Xanthoma Tuberosum Multiplex. Presented by DR. MAX SCHEER.

J. L., a man aged 50, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 4, 1941, with cutaneous lesions of two years' duration. The family and personal histories were normal. He has been in good health except for "tightening of the calf muscles on walking" for about a year and occasional tremors of both hands. The patient is of strong physique, about 5 feet 4 inches (163 cm.) in height, weighing 195 pounds (88.5 Kg.) and in apparent good health.

The eruption started about two years ago as small wartlike growths. They remained stationary until six months ago, when they grew to the present size, but they have not grown appreciably since. These lesions are not in the least disturbing to the patient. They never showed any tendency to involution.

On the extensor surface of the left elbow joint are two lentil-sized nodules. Located at and below the right olecranon process are seven match head–sized to large pea–sized, fairly hard, chamois–colored, raised, discrete and well marginated nodules. The skin covering all of these lesions is smooth, stretched and tense but intact except for one, which is crusted. The nodules are painless and freely movable, the smaller being rounded and the larger flat topped.

The routine laboratory tests gave negative results except for a leukocyte count of 15,000 and an increase of the lipid constituents of the blood, as follows:

Total cholesterol amounted to 415 mg. (normal 160 to 230 mg.) per hundred cubic centimeters, with 335 mg. (normal 100 to 150 mg.), or 80 per cent (normal 40 to 60 per cent), cholesterol esters.

The histologic section examined by Drs. Satenstein and Sachs showed a picture of xanthoma.

DISCUSSION

DR. DAVID BLOOM: It would be of interest to study the carbohydrate metabolism in this patient.

DR. GEORGE C. ANDREWS: I do not think that internists appreciate the importance of the relation of intermittent claudication and coronary occlusion to xanthomatosis and high blood lipids. This patient has such a combination. All his life he has been eating for breakfast two eggs and bacon with lots of butter. In other words, he has been on a high fat diet. I do not think that the internists appreciate generally that by taking such patients off this diet they can frequently cure intermittent claudication and relieve the symptoms of coronary occlusion. A history of bilious attacks and of gallstones also is common for this group of patients. Such reports are in the literature, but few internists of my acquaintance seriously treat coronary occlusion by low fat diet.

DR. HERMAN SHARLIT: What Dr. Andrews said is perfectly right. As far as treatment is concerned, all such patients do well on a diet in which all animal fats are absolutely excluded, plus the administration of thyroid.

DR. MAX SCHEER: At the meeting of the Academy of Dermatology and Syphilology in Philadelphia, Dr. Montgomery gave a talk on the relation of xanthoma tuberosum and coronary disease. He said that coronary disease was common in patients with xanthoma. What the relation is between this patient's intermittent claudication and his xanthoma I am unable to say. His intermittent claudication might be due to many other causes, tobacco, for example.

Lichenoid Dermatitis Following Arsphenamine. Presented by DR. GEORGE C. ANDREWS.

J. M., a white man aged 50, is presented with lichenoid dermatitis of the axillas, groins, cubital spaces, right popliteal space and trunk. The individual lesions are papulonodular and brownish and vary in size from that of a pea to that of a dime. Some of the lesions are flat-topped papules closely resembling those of hypertrophic lichen planus. They itch rather intensely at times.

This patient was seen first this afternoon and gave the history that he has been taking antisyphilitic treatment for two years, including neoarsphenamine and a bismuth compound. The eruption appeared about six months ago and has been getting progressively worse. The general health has been good, and the syphilis, for which he had been treated, was presumably a latent infection which was discovered on routine blood testing. There is no history of ingestion of drugs.

DISCUSSION

DR. SAMUEL PECK: If I had a patient with a lichen-planus-like eruption due to arsenic (and many of them have been reported), I certainly should not give any more of the arsphenamine, and the condition surely should get worse, if it coincides with past experiences with these eruptions. According to the French authors, when lichen planus or pityriasis rosea or even a psoriasiform eruption follows administration of one of the arsphenamines or arsenic, the condition is not a true arsphenamine eruption but an eruption that is due to the same cause as lichen planus or a pityriasis rosea-like eruption which has been awakened or become activated by the arsenic, and they did not hesitate to recommend giving more arsenic. That was written before it was known that patients could become sensitized with arsenic and that it could produce such eruptions. Dr. Satenstein once made the remark that the differential diagnosis histologically between true lichen planus and that due to arsenic was that in lichen planus due to arsenic one could find the arsenic deep in the cutis.

DR. WILBERT SACHS: Histologically it is difficult to differentiate the usual lichen planus from that due to arsenic. It is not a matter of depth. There are more edematous changes in the vessels which do not occur in ordinary lichen

planus and also more wandering connective tissue cells in the cellular infiltration. The usual variety of lichen planus is the same as lichen planus lesions following the taking of arsenic except for the changes about the vessels, the presence of more wandering connective tissue cells and perhaps some changes in the epidermis.

DR. E. WILLIAM ABRAMOWITZ: This eruption appeared primarily without any previous arsenical dermatitis. In many of the patients an arsenical exfoliating dermatitis first develops, and when the eruption is subsiding the lichen planus eruption appears. The administration not only of arsenic but also of other heavy metals should be discontinued. If a patient gets an eruption after gold therapy, I cannot say that the patient is going to have an eruption from other heavy metals. That does not necessarily happen in the same patient; nevertheless, one has to be cautious about using other heavy metals, as multiple hypersensitivity may be present or may develop.

DR. M. B. PAROUNAGIAN: I question whether this condition is due to arsenic. I have a patient now who has not received any arsenic but who has the eruption in the same location with the same clinical appearance that this patient presented tonight. I think the condition is due to fungous infection.

DR. GEORGE M. LEWIS: Without the benefit of the history and solely on clinical grounds I should be in favor of a diagnosis of a lichenoid eruption rather than lichen planus because of the distribution, which would be atypical for lichen planus on account of the absence of lesions on the mucous membranes, and because there are no definite lichen planus papules. Since there is a history of ingestion of arsenic, such an etiologic possibility must be considered.

DR. HOWARD FOX: This patient has been getting arsphenamine for six months, and it has not done him any apparent harm. I see no reason to discontinue giving this drug, if it is thought that he requires it.

DR. MAX SCHEER: I agree that in this type of eruption it is safe to continue arsenical therapy.

DR. J. FRANK FRASER: I presented a patient in January at a meeting of the New York Dermatologic Society (ARCH. DERMAT. & SYPH. **44**:510 [Sept.] 1941) with a similar history and similar lesions. The histologic observations in that case and in this case were those of lichen planus. Two days ago a brother of my patient appeared with exactly the same history and an eruption identical with that of his brother's except that it was not so extensive.

In regard to the case presented, I am inclined to agree with the members who saw lesions which could be designated from a clinical point of view as straightforward lichen planus, especially those in the axillas. Dr. Lewis' objection that there are no lesions on the mucous membrane does not exclude the diagnosis of lichen planus. Lesions of the mucous membrane occur only in about 50 per cent of the cases of lichen planus, and most frequently in the acute generalized variety. My experience in studying sections of lichenoid dermatitis has been that the histologic picture is always identical with that of lichen planus. Dr. Peck referred to the theory of the French that the administration of arsenic may excite to pathogenicity the latent unknown cause of lichen planus.

DR. GEORGE C. ANDREWS: The patient came to me today for an opinion because he thinks that every time he gets an injection of arsphenamine it makes him itch worse. This patient apparently had no preceding eruption but did have severe pruritus for eighteen months before the lichen planus eruption developed. I think one must differentiate lichen planus following arsphenamine therapy from a lichenoid dermatitis of an arsenical character or eczema due to arsenic (lichenified arsenical eczema). It is the practice at Vanderbilt Clinic in cases of lichen planus following arsphenamine treatment to continue the treatment with arsphenamine, but in those cases there is no itching. This case is different because there was violent itching after the injections of arsphenamine. I suspect that this condition is lichenoid dermatitis due to arsphenamine sensitization, and I believe it is injurious to give him arsphenamine. His skin is getting worse, and he attributes the fact that it is growing worse to the arsphenamine.

Common Warts Cured by Mental Suggestion. Presented by Dr. Howard Fox.

C. K., aged 16, a delivery boy, was first seen by me on July 19, 1940. He had suffered for the past year from common warts on the backs of the hands. There were fifty-two of these lesions, which varied in size from that of a millet seed to that of a split pea. He had previously been treated for the warts by seven "injections" at the dispensary of Lenox Hill Hospital.

His hands were placed under an x-ray tube, the filament being lighted but no roentgen ray treatment being given. He was asked to return in a month and assured that he would then be free of warts in all probability. Unwittingly, he was given an ointment of ammoniated mercury containing 3 per cent of salicylic acid. When seen two weeks later there was great improvement in the lesions, and on his next visit two weeks later all except eight or ten of the lesions had disappeared without a trace or at most with only a slight depigmentation. The remaining eight lesions gradually disappeared during the following month. A single lesion remained at the end of the fourth month and was removed by curetting under local anesthesia.

There has been no recurrence of any of the lesions, and no new ones have appeared up to the present. The patient was a healthy, normal-appearing boy.

DISCUSSION

Dr. David Bloom: Verrucae planae are not infrequently a major complaint. Psychotherapy is a worth while method, particularly in children. I have had success in numerous children and in 2 medical students.

Dr. Max Scheer: Some years ago I treated a group of 50 children at the Hebrew Orphan Asylum who had verrucae vulgares, mostly on the hands, and tried psychotherapy. These children were all brought into my room from another room after being blindfolded. I painted eosin on the warts and pressed them rather firmly and made notes as to whether the children showed any emotional reaction. Some cried, some were frightened and some did not mind it at all. In four weeks I reexamined them, and in 40 per cent the warts had disappeared. That did not surprise me. What did surprise me was that a mole on the nose of 1 child, which had been there since the child's birth, had disappeared.

Dr. Howard Fox: I do not think there is any doubt that warts may disappear as a result of mental suggestion. That has been definitely proved by Bloch, and Dr. Scheer has just cited a large series of successful results. I have tried Dr. White's suggestion of treating flat warts, which consists of the oral administration of protoiode of mercury. I have often wondered whether it was the mercury or the suggestion that cured the disease in children or adolescents, because I have usually told them that they would be entirely well in three or four weeks. Children are naturally more impressionable than adults and are more receptive to suggestion.

J. Frank Fraser, M.D., *President*

Anthony C. Cipollaro, M.D., *Secretary*

May 13, 1941

Inoculation Tuberculosis of the Skin. Presented by Dr. E. William Abramowitz.

P. F., a boy aged 9 years, is presented from Gouverneur Hospital (surgical service of Dr. M. G. Elias) with an eruption on the left thigh and shin. The first lesion appeared on the left shin about seven months ago and was attributed to scraping the shin against the stairs. Four months ago an abscessed gland developed over the area of the left Scarpa's triangle, which was opened and then excised. The present granulating wound followed the excision.

The lesion on the shin shows a series of small aggregated papules on a coppery base, forming a penny-sized plaque. The histologic report showed tuberculosis cutis.

The histologic report of the excised femoral gland showed typical caseating tubercles. Inoculation of a piece of gland tissue into a guinea pig revealed tuberculosis on autopsy. The tuberculin test elicited a mildly positive reaction with a dilution of 1 : 10,000, and the roentgenogram of the chest showed slight hilar and central root branch thickening (old healed tuberculosis).

Pityriasis Lichenoides et Varioliformis Acuta. Presented by DR. MAX SCHEER for DR. ALBERT SCHUR.

C. P., a man aged 41, born in the United States, was first seen on March 6, 1940, when he presented an eruption of four weeks' duration on the entire trunk and lower extremities. The lesions consisted of raised, dull red, crusted and ulcerated papules varying in size from that of a match head to that of a cherry. Other older lesions were surmounted by a dry, firmly embedded scale, and some are capped with vesicopustules on a dark purplish red necrotic-looking base.

They have increased in number since inception, starting as a few scattered lesions and spreading in crops to involve the entire trunk and upper and lower extremities but leaving the head free. This continued for nine months, when a definite thyrotoxicosis developed. He was admitted to St. Joseph's Hospital for the latter condition, where a thyroidectomy was performed and he made an uneventful recovery. After the operation, on Dec. 22, 1940, he had a period of quiescence, and the lesions were scarce, scattered and considerably smaller. However, one month later there was a relapse, and crops of identical lesions have continued to appear in ever increasing numbers. On Jan. 28, 1941 two pustular, hemorrhagic, crusted lesions appeared in the center of an old vaccination scar, and during the last month lesions have been appearing on the face, including the eyelids, and on the penis.

The patient now presents hundreds of varioliform scars at sites of healed lesions. He has received sodium arsenate, injections of sodium cacodylate, a high vitamin intake (ViPenta) and 3 vaccinations, the first of which "took" on Feb. 18, 1940 and the others on March 24 and April 19.

The blood picture and the urine were normal, and the Wassermann reaction was negative. A biopsy was done on April 13, 1940, and the histologic picture was reported as consistent with parapsoriasis varioliformis by Dr. Charles Miller and confirmed by Dr. Satenstein.

DISCUSSION

DR. ISADORE ROSEN: I should hesitate to accept the pathologic diagnosis of pityriasis lichenoides et varioliformis acuta, as I see no evidence of this disease. The impression I get is that the patient has a drug eruption (iodides or bromides) or some bacterial infection of the skin.

DR. E. WILLIAM ABRAMOWITZ: A toxic goiter developed in the course of this eruption; so I believe this cutaneous condition is some form of toxic eruption. I think that this patient should be observed further and particularly that a blood count should be made.

DR. FRED WISE: My impression is different from that of Dr. Rosen's. To me it seems that the correct clinical diagnosis is parapsoriasis lichenoides.

DR. DAVID BLOOM: In spite of the unusually large lesions on the back of the patient I favor the diagnosis as presented. The fact that the patient has hyperthyroidism and underwent a thyroidectomy interests me greatly. I recently treated a girl for pityriasis lichenoides et varioliformis who had definite exophthalmos. The basal metabolic rate was normal. I believe that thyroid dysfunction possibly plays a role in this disease.

DR. WILBERT SACHS: The varioliform lesions in this disease and the varioliform lesions in chickenpox and smallpox are entirely different. Clinically, they

look alike, but pathologically they do not. In chickenpox there is a degenerated epidemic vesicle or pustule. There are two varieties of varioliform lesions in pityriasis varioliformis; one is urticarial, without many cells, and the other has little edema but is full of cells. The latter is more apt to become necrotic. While clinically lesions of chickenpox and pityriasis lichenoides et varioliformis acuta may be similar, pathologically they can be differentiated. In pityriasis lichenoides et varioliformis acuta there is also the microscopic picture of parapsoriasis.

DR. MAURICE J. COSTELLO: I have observed several patients suffering from this dermatosis at Bellevue Hospital who improved with fever therapy, typhoid vaccine having been administered intravenously in graduated doses.

DR. ALBERT SCHUR (by invitation): This case was presented for several reasons, first of all because of the chronicity of the condition and the occurrence of more lesions within the past month than there were three or four months ago. Clinically I could not conceive of any other diagnosis except pityriasis lichenoides et varioliformis acuta because the lesions looked typical. Some of the lesions before becoming necrotic looked like the lichenoid type of parapsoriasis. They were fiery red and surmounted by pustulovesicles. They became necrotic and ulcerated, and, what seems to be more characteristic, there are now typical varioliform scars. As a matter of fact, the patient was vaccinated three times and the first vaccination "took," and it is almost impossible to tell the difference between a vaccination scar and a varioliform scar resulting from his disease. Another reason for presenting him was for suggestions as to therapy. He has been treated for fifteen months, and instead of showing signs of recession more symptoms are developing. Until the past month he never had itching, and now he is uncomfortable. He never had lesions on the face until lately, and now he even has lesions on the penis and on the eyelids. It was thought that some one would suggest the possibility of treating him with sulfanilamide. The reason that entered my mind is that several diseases, like Duhring's disease and herpes, present lesions somewhat similar and have been reported as responding to treatment with sulfanilamide and its derivatives.

Extensive Lupus Erythematosus in a Child Following Excessive Exposure to the Sun. Presented by DR. PAUL E. BECHET.

L. R., a girl aged 5 years, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. She has been excessively exposed to the sun for several years. One year ago a dime-sized, angry red, infiltrated spot appeared below the right lower eyelid. During the past six or seven months new lesions have rapidly appeared.

At present there are patches on the forehead extending to within the hair line, with large patches on both cheeks and on the nose. More than half of the face is covered with the characteristic purplish red, raised, somewhat infiltrated and scaly patches of the subacute discoid type of lupus erythematosus. On close examination patent follicles and fine telangiectases are observed. There are numerous pinhead-sized to pea-sized satellite lesions around the large patches. The buccal mucosa is not involved. The general health is good.

Roentgenograms of the lungs demonstrated a moderate hilar and central root branch thickening, with lymphoid deposits in the midpulmonic field. The porphyrin content in the urine was normal. Histologic examination showed in the upper part of the cutis and about the adnexa a moderate cellular infiltrate. There was considerable edema in the subepidermic region with some washing out of the basal cell margin above. The rest of the epidermis was somewhat thin. The vessels were round and filled with horny plugs. The cellular infiltrate had small round and wandering connective tissue cells. There was no basophilic degeneration. The elastic tissue showed some fragmentation but no clumping.

A Case for Diagnosis (Granuloma Annulare?). Presented by DR. WILBERT SACHS.

W. S. M., a white man aged 28, stated that the eruption began in the middle of February on the right side of the chin with one small red spot which gradually spread and became larger. Since that time other lesions have appeared somewhat the same way.

The patient now presents on the right side of the chin and extending into the corner of the mouth, a large circular area (a little larger than a silver dollar) with a definite infiltrated border all around and with a slightly clearer center. There is no scaling. On either side of the nose there is a similar lesion, somewhat smaller, with an infiltrated border and with some infiltration in the center. On the left side of the cheek, at the angle of the jaw, there are two similar small circular lesions, one in the center of the left cheek and one in the center of the right cheek just in front of the ear. There is one lesion on the right side of the neck and one on the forehead, just above the right eye.

The microscopic picture was that of granuloma annulare.

Lupus Miliaris Disseminatus Faciei. Presented by DR. HERMAN SHARLIT.

S. E., a woman aged 48, first came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in March 1941 with an eruption on the forehead and cheeks of seven months' duration.

The patient now presents on the forehead and symmetrically disposed on the cheeks numerous pinhead-sized to lentil-sized erythematous papules, pustules and particularly crusted lesions.

A tuberculin test elicited a negative reaction with a dilution of 1:10,000. A roentgenogram of the lungs revealed no abnormality except slight thickening of the hilus and central root branch. The Wassermann reaction of the blood was negative, and the urine was normal. Examination of the blood showed: erythrocytes, 4,750,000; hemoglobin, 90 per cent; leukocytes, 12,300; neutrophils, 80 per cent; basophils, 1 per cent; monocytes, 7 per cent, and lymphocytes, 12 per cent. A biopsy was made, and the histologic diagnosis was lupus miliaris faciei.

DISCUSSION

DR. SAMUEL PECK: While the patient may have a lupus miliaris it is difficult to make the diagnosis clinically. In the classic examples of this condition individual lesions are more isolated and scaly crusted eruptions are not seen. The condition in the majority of instances is self limited. This is strange, since in many of the cases which have a spontaneous remission, the guinea pig inoculations give positive reactions for tuberculosis. It is in this group of cases that the reaction to the tuberculin test is negative. I have reported such cases (Beitrag zur Lehre vom Lupus miliaris disseminatus faciei, *Arch. f. Dermat. u. Syph.* **158**:545, 1929).

DR. MAURICE J. COSTELLO: Is it not also true that in lupus miliaris disseminatus faciei lesions are almost invariably seen on the mucous membrane of the lips?

DR. WILBERT SACHS: There is definite necrosis in the center of the lesions. This is a feature of lupus miliaris faciei rather than of rosacea-like tuberculid of Lewandowsky. Therefore, I agree with the diagnosis as presented.

DR. SAMUEL PECK: Lewandowsky has given one of the best differential diagnoses between lupus miliaris and lupus vulgaris, both histologically and clinically. In some instances it is difficult to make a differential diagnosis. As a matter of fact, he made the statement that the classic tubercle histologically is found more often in lupus miliaris than in lupus vulgaris.

DR. HERMAN SHARLIT: The diagnosis is definitely established, even though one feels that clinically it does not look like the condition suggested. This diagnosis has to be accepted, since it is made histologically.

Erythema Annulare Centrifugum. Presented by Dr. George M. Lewis.

B. B., a white man aged 22, is presented from the New York Hospital. He stated that an eruption appeared four months ago and has gradually spread on both legs below the knees. There have been no subjective symptoms. The patient has had a congenital cardiac disease with cyanosis since birth. The fingers show clubbing. There is no history of ingestion of drugs.

On the legs below the knees are configurate, irregularly shaped plaques with no central clearing. The plaques are elevated with sharply defined edges. There is some sloping down from the borders toward the inside of the lesions. The color is dusky red; it is thought that it is partly influenced by the congenital cardiac lesion. This color cannot be entirely pressed out by the diascope. The margin of a lesion was shown to have advanced over ¾ inch (2 cm.) in three weeks.

The examination for tinea gave negative results. There was no reaction to trichophytin. The biopsy section showed vascular dilatation, considerable edema and a perivascular infiltrate mainly composed of lymphocytes.

DISCUSSION

Dr. E. William Abramowitz: I think that this case is most unusual. The deep cyanotic coloring can be explained by the presence of the congenital cardiac condition. I agree with the diagnosis as presented.

Dr. Fred Wise: The eruption bears only a superficial resemblance to erythema centrifugum, but I believe the condition is directly related to some underlying constitutional disease.

Leukoderma with an Inflammatory Border. Presented by Dr. Fred Wise.

C. D., a woman aged 47, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 3, 1941 complaining of white patches of eight weeks' duration. A silver dollar–sized red ringlike rash first appeared on the volar surface of the right wrist preceded by itchy sensations. She painted it with iodine. Five days later the patient noticed a white area occupying the entire ring. Three to four weeks later slightly scaly red solid spots appeared on the middle of the backs of both forearms; these have been spreading upward toward the elbows and white spots without rings appeared in the left clavicular region. These spots clear in the center, forming areas which enlarge by peripheral extension and by coalescence of the individual lesions. The red rings undergo involution within three or four weeks, leaving the depigmented areas, which "seem to be permanent."

Seven years ago a hysterectomy was performed for a uterine fibroid. There is no history of other cutaneous diseases except for a scaly vesicular patch in 1926 on the right thenar eminence. She had been taking "alka seltzer" and acetylsalicylic acid occasionally for headaches and medicines for "poor circulation and nerves" for four weeks prior to the eruption. For the past six months she has been nervous, but her general health has otherwise been good. In her work as chamber maid she has been frequently using ammonia and scouring powder. Four weeks ago a similar spot, 3 by 3 inches (7.5 by 7.5 cm.), appeared on the front of the neck.

On the volar surfaces of the wrists and forearms are well defined snow white spots of normal texture. They are round, oval and irregular and vary in size from that of a pea to 6 by 10 cm. Either a distinct red slightly raised and finely scaling border 2 to 3 mm. in width, as seen on the front of the neck, or broken incomplete rings edge the inner sides of the spots on the forearms. On the dorsal aspect of the right hand and on the left palm are moderately infiltrated, irregular, well marginated, hyperkeratotic, slightly crusted solid patches with some fine fissuring. There is a poorly defined, erythematous, superficial patch 10 cm. in length on the right calf.

The results of routine laboratory tests, including chemical examination of the blood, were normal except for a leukocyte count of 4,800 per cubic millimeter, with 36 per cent polymorphonuclear neutrophils and 40 per cent lymphocytes. Scraping of the borders of the lesions on the neck and forearms were examined and cultured and found negative for fungi.

A section taken from the border of a lesion on the forearm was stained with hematoxylin and eosin and examined by Dr. W. Sachs. He diagnosed the condition as a "neurodermatic reaction" and described it as follows: "In the middle and upper parts of the cutis the vessels are dilated, and about them is a moderate focal cell infiltrate composed of small round cells and wandering connective tissue cells. There is a moderate interstitial edema throughout the entire cutis. The epidermis is somewhat acanthotic, and the palisade layer is intact throughout. The granular and horny layers are present. There is no edema in the epidermis."

Patch tests with scouring powder and brown laundry soap elicited 2 plus reactions.

The patient was advised to avoid coming in contact with irritating substances, to use a neutral soap for cleaning and to apply magnesium and zinc carbonate lotion locally. She was seen again on May 26, 1941; there were no new leukodermic patches evident, and the inflammatory borders had entirely disappeared.

DISCUSSION

DR. HERMAN SHARLIT: I agree that there is depigmentation.

DR. DAVID BLOOM: Recently I observed leukoderma in the axillas of a woman who had a ring of dermatitis around the axillas. In spite of negative reactions to patch tests with black dress material and rubber shields, I considered the black dress as the cause of the dermatitis, as not wearing the dress led to improvement of the eruption while wearing the rubber shields did not exacerbate the condition. I believe, therefore, that not only rubber material may produce leukoderma, as described by Oliver, Schwartz and Warren (ARCH. DERMAT. & SYPH. **42**:993 [Dec.] 1940), but also any other irritant which causes dermatitis may lead to leukoderma.

DR. SAMUEL PECK: The latest work with antioxidants has revealed the cause of leukoderma in some interesting cases. One patient had depigmentation in both axillas which I was able to attribute to agerite alba (monobenzyl ether of hydroquinone) in dress shields. Another patient was a young girl with scattered depigmented areas on the back, which also were due to an antioxidant found in the rubber mattress she was using.

A Case for Diagnosis (Reticulated Hyperpigmentation and Depigmentation of the Face?). Presented by DR. MAURICE J. COSTELLO.

A. B., a Puerto Rican housewife aged 38, is presented from Bellevue Hospital. She presents a generalized, symmetric, nonpruritic eruption which has been continuously present for the past fifteen years. It consists principally of reticulated areas of hyperpigmentation and depigmentation on a dull erythematous background and is confined to the affected areas. She complains of pains in the knees and ankles and occasionally of swelling of the knees, ankles and finger joints. She has attacks of angioneurotic edema and asthma.

Her blood pressure is 160 systolic and 110 diastolic. The Wassermann reaction of the blood was negative. Her hemoglobin determination was 70 per cent. The erythrocyte count was 4,710,000 per cubic millimeter, and the leukocyte count was 7,600, with 58 per cent polymorphonuclear leukocytes, 37 per cent lymphocytes and 5 per cent eosinophils. Roentgenograms of the heart and lungs showed slight accentuation of the left ventricular curve, widening of the supracardiac aorta and diffuse congestive changes in both lungs. The basal metabolic rate on June 19, 1940 was —11 per cent and on July 26, 1939 +3 per cent. Roentgenograms of the hands showed no osseous changes. The reaction to a patch test with tuberculin (Lederle) on the inner aspect of the left arm was positive (reaction being folliculo-

papular) after forty-eight hours, and reactions to intradermal tests with old tuberculin in 1 : 1,000,000 and 1 : 100,000 dilutions were positive after forty-eight hours, 1 plus and 3 plus respectively. Histologic examination was of no help in determining the nature of this dermatosis.

DISCUSSION

DR. FRED WISE: I have no diagnosis to offer, but I think Dr. Costello will be interested to know that there is a good illustration of the same type of reticulated pigmentation in the Jadassohn handbook (Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 4, pt. 2, p. 859), also in L. Nékám's "Corpus Iconum Morborum Cutaneorum" (Leipzig, Johann Ambrosius Barth, 1938, pt. 3, p. 595), labeled morbus albomacularis.

DR. HERMAN SHARLIT: Is it depigmentation or hyperpigmentation that causes this? The patient has a light skin, and I think the effect is due to increased pigment rather than decreased pigment.

DR. SAMUEL PECK: The reticulated type of pigmentation is most often found after ingestion of arsenic. However, other heavy metals have sometimes caused this same type of pigmentation. The drug may have to be taken for a long time before pigmentation becomes evident. In conditions following arsenic medication, it is solution of potassium arsenite U. S. P. which is most often at fault.

DR. MAURICE J. COSTELLO: Somebody made the observation that the creases in the neck do not show hyperpigmentation and that the hyperpigmentation is confined almost entirely to exposed areas; the creases in the neck are naturally shielded from sunlight.

A Case for Diagnosis (Multiple Fibromas?). Presented by DR. FRED WISE.

H. G., a man aged 49, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 29, 1941, with cutaneous growths of six years' duration. His father died of cancer of the throat. The family history was otherwise irrelevant. The patient enjoys general good health. His weight has been stationary for the past few years. He is being treated now for a "sinus condition."

One or two nodules appeared first about six years ago at the left alar sulcus. Since then other nodules have been slowly developing, spreading progressively downward on the lip and laterally to the left cheek. There are no subjective symptoms.

Occupying the upper two thirds of the left half of the upper lip, the entire left nasolabial groove, the upper half of the philtrum, which is somewhat deflected toward the right cheek, and the floor of the right anterior naris are round and ovoid, lentil-sized to pea-sized, skin-colored and pinkish soft nodules over which the skin is intact. Some nodules are discrete, while others are fused only at the bases and have projecting summits. Over some of the nodules are seen fine telangiectatic ramifications. Moderate diascopic pressure resulted in a leveling of these growths, leaving a uniform white skin with telangiectases. There is a fulness of the left portion of the upper lip which is slightly lower than the right. The mucous membrane on the inside of the lip opposite the growths is smooth. There is an irregular, reddish yellow, slightly raised plaque about 2.5 by 2 cm. in diameter on the posterior half of the left side of the palate.

In the vestibule of the mouth on the left side of the gum of the upper jaw extending from the proximal surface of the lateral incisor to the distal surface of the first premolar is an ill defined growth of which the patient was unaware. It is the size of a finger nail, 2 to 3 mm. in thickness, fairly hard, nontender and smooth. There are no other lesions on the integument.

The results of routine laboratory tests, including chemical examination of the blood, were normal. The roentgenographic report of the left maxillary area was as follows: "Examination directed to the superior and inferior maxilla shows insufficient evidence of gross pathologic change to be of roentgen diagnostic value. The diagnosis was negative."

Histologic sections of a nodule taken from the lip stained with hematoxylin and eosin and examined by Dr. W. Sachs showed "fibroma," and sections of the growth on the gum "might fit in with lymphangioma." Description of the nodule taken from the lip was as follows: "In the center of the section and extending throughout the entire cutis is a definite increase in the connective tissue. There is a diffuse cellular infiltration of spindle-shaped cells. In a few areas there is a focal cellular infiltration. The overlying epidermis shows no important changes." Description of the lesion on the gum was as follows: "Throughout the cutis are numerous dilated lymphatic vessels. There are also numerous congested blood vessels. The entire cutis is loose and lacy. In the center of the section is a large vessel, the lumen of which is filled with fibrous tissue and spindle-shaped cells."

The fibromas were exposed to fractional roentgen rays once weekly. A total of 1 unit filtered through 1 mm. of aluminum (450 r) was thus far given. There seems to be some but not yet definite evidence of involution of these growths.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: Was there not a lesion on the hard palate on the left side with a yellowish tinge? I think a possible fibroxanthoma ought to be ruled out.

DR. WILBERT SACHS: I should like to venture a diagnosis of Recklinghausen's disease. I do not believe the condition is a sarcoma. Tissue taken from a deeper part of a lesion may show a different process.

DR. FRED WISE: The histologic picture was that of fibroma.

Chronic Lymphangitis (Syphilis) of the Lower Lip and Chin. Presented by DR. E. WILLIAM ABRAMOWITZ.

G. H., a man aged 55, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in October 1939, with a history of having had syphilis twenty years previously, for which he received treatment and was apparently cured, judging from the results of tests of the blood and spinal fluid. About four years ago the present eruption began on the lips, and it gradually spread down to the chin.

He was presented on Oct. 3, 1939 at a meeting of the Section of Dermatology and Syphilis of the New York Academy of Medicine (ARCH. DERMAT. & SYPH. **41**:767 [April] 1940). He had an erythema and edema of the right side of the lip and chin with numerous elevated vesicular and verrucous-like lesions. The Wassermann reaction of the blood and that of the spinal fluid were negative. The colloidal gold curve of the spinal fluid was normal. Urinalysis gave normal results. Examinations for fungi, by both microscopic and cultural methods, failed to reveal any. Histologic examination showed a superficial dermatitis with a cellular infiltration, predominantly of plasma cells.

Since then the patient has had Frei tests and search has been made for the presence of virus infection, both of which gave negative results.

He received a bismuth compound, arsenic, antimony and potassium tartrate, fuadin and sulfanilamide and its derivatives, with little benefit.

The patient is presented showing considerable improvement following about seven or eight febrile attacks from the use of typhoid vaccine.

DISCUSSION

DR. FRED WISE: I accept the pathologic diagnosis of lymphangitis, but I think the entire process is due to syphilis. Fournier described such cases.

DR. MAURICE J. COSTELLO: At Bellevue Hospital I observed patients with 4 plus Wassermann reactions who presented recalcitrant lesions which did not respond to the usual treatment and whose conditions were improved by rubbing ointment of mild mercurous chloride N. F. directly into the lesion.

DR. DAVID BLOOM: If these lesions do not correspond to antisyphilitic therapy it follows that they are not really syphilitic. At most one could suspect a sequela of syphilis.

DR. E. WILLIAM ABRAMOWITZ: I do not deny that this man had syphilis. Apparently his treatment was adequate, for he is in good health, except for the lesion on the lip, and his serologic reactions are negative. The fever therapy was undertaken as a nonspecific measure, as various other methods proved ineffective. Further biopsies will be made, and this man will be observed further.

NOTE.—Two biopsy specimens were later taken from different portions of the affected area on the lower lip. Dr. W. Sachs reported that the infiltration was characteristic of syphilis. The lesions improved still further under treatment with injections of bismuth subsalicylate.

Lupus Vulgaris with Complicating Synovitis. Presented by DR. MAURICE J. COSTELLO.

F. A., a man aged 74, from Bellevue Hospital, states that the eruption has been present for two years, and he has complained of chronic cough for several years.

He has a rectangular, well circumscribed eruption, consisting of numerous pinhead-sized, apple jelly nodule infiltrations, interspersed with small strands of scar tissue. In the center of the lesion there is an irregularly shaped ulcer which is attached to the sheaths of the flexor tendons. When the fingers are extended there is a retraction of the involved area of the skin.

A roentgenogram of his chest showed thickening of the basal pleura on the right side and dense bilateral perihilar fibrosis. The Wassermann reaction of the blood was negative. Histologic examination showed changes consistent with tuberculosis cutis. The reaction to a patch test with tuberculin (Lederle) was positive after forty-eight hours, being a folliculopapular eczematoid reaction. Graduated intradermal tests with old tuberculin in 1:1,000,000 and 1:100,000 dilutions elicited 2 plus and 4 plus reactions respectively.

Lichen Planus in a Scar. Presented by DR. GEORGE M. LEWIS.

J. L., a white chauffeur aged 25, is presented from the New York Hospital. He first noticed a rash one month ago. The first lesions appeared in scar tissue on the anterior part of the left forearm. The scar tissue on the arm is the result of a chemical burn in January 1938. New lesions have appeared in normal skin on the arms and legs.

Examination shows typical lichen planus papules both in the scar tissue on the left forearm and on the legs. On the left forearm there is a definite predilection for the scar tissue over normal tissue. Lesions are present on the mucous membrane of the mouth.

The histologic examination of biopsy tissue confirmed the diagnosis.

DISCUSSION

DR. MAURICE J. COSTELLO: I treated several patients with vitiligo at Bellevue Hospital by giving weekly injections of gold sodium thiosulfate in doses up to 50 mg. In a few a lichenoid eruption developed. The lichenoid papules were found only in vitiliginous areas. Maybe the lack of pigmentation has something to do with it.

Chronic Disseminated Lupus Erythematosus. Presented by DR. FRED WISE.

F. P., a coal miner aged 46, with generalized cutaneous lesions, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 1, 1941. He was referred by Dr. S. R. Kaufman, of Wilkes-Barre, Pa. The patient gives no family history of cutaneous or allergic diseases.

He does not recall ever having fever or pains in the joints. An appendectomy was performed in 1911, and the tonsils and adenoids were removed in 1931. Recently he had three teeth extracted. He feels generally well except for pruritus.

In the spring of 1927 an itchy, red, scaly rash appeared in the malar regions and at the root of the nose distributed in a butterfly fashion. It cleared up in the fall but reappeared the following spring and has persisted since, slowly but progressively spreading until both cheeks have become completely involved. In October 1940, after several generalized ultraviolet exposures and ingestion and topical application of sulfanilamide, an erythematous eruption developed suddenly on the neck, trunk and upper and lower limbs.

The patient is 5 feet 6 inches (168 cm.) in height and weighs about 140 pounds (63.5 Kg.). He presents a generalized eruption on the face, scalp, trunk and upper and lower extremities. The upper half of the trunk, except for the axillary regions, is almost completely enveloped with diffuse, purplish red, superficial, slightly scaly sheets, sharply differentiated from the lower half of the trunk and lower limbs. The lesions in the latter areas consist of discrete brownish red patches varying in size from that of a pea to that of a finger nail or palm. The face, scalp margins and ears are similarly affected. The ear lobes are atrophic, shrunken and sclerotic. Some patches are smooth, shiny and edematous; others are slightly depressed, finely wrinkled, atrophic and covered with sparse scaling. Many lesions reveal on close examination dilated follicles and telangiectases. There is a diffuse alopecia of the scalp and a total alopecia of the cheeks.

The hemogram showed a leukocyte count of 5,050, a red cell count of 4,130,000 per cubic millimeter, 51 per cent polymorphonuclear neutrophils and 36 per cent lymphocytes. The icterus index was 7.9 units. The other routine laboratory tests, including testing of blood for cholesterol, gave negative results. Examination of the urine for coproporphyrin (Zeligman) showed a total of 210 micrograms in a twenty-four hour specimen (2,500 cc.). This is equivalent to 3.3 micrograms per kilogram of body weight per twenty-four hours (maximum normal is 3 micrograms per kilogram per twenty-four hours). A tourniquet placed about the left arm caused a denudation of the epidermis of a 2 by 2 cm. area. The roentgenogram of the chest was normal.

A histologic section stained with hematoxylin and eosin and examined by Dr. Sachs showed: "Toxic dermatitis (might fit in with acute or subacute disseminated lupus erythematosus). The epidermis is missing. The vessels of the upper and middle portions of the cutis are dilated, and some are filled with blood elements. There is in part a diffuse and in part a focal cellular infiltration of small round cells, many wandering connective tissue cells and some plasma cells. There is pronounced interstitial edema throughout the upper part of the cutis. There is no basophilic degeneration. Weigert's elastic tissue stain showed no important change."

NOTE.—The patient was admitted to the New York Post-Graduate Medical School and Hospital on May 1, 1941. He was treated with topical applications of Burow's emulsion (aluminum acetate solution, 6 cc.; zinc oxide, 12 Gm.; talc, 12Gm.; olive oil, 15 cc., and solution of calcium hydroxide, a sufficient quantity to make 120 cc.), daily injections of 1 cc. of liver extract (2 U. S. P. units per cubic centimeter) and intramuscular injections of 1 cc. of bismuth subsalicylate (0.13 Gm. per cubic centimeter) every five days. During his stay at the hospital his temperature (rectal) varied from 97 to 99.2 F. and at one time reached 101.5 F. He was discharged on May 23, 1941, feeling somewhat better, though there was no appreciable change in his condition.

DISCUSSION

DR. WILBERT SACHS: My clinical diagnosis would be discoid type of lupus erythematosus, but microscopically the picture is that of a severe toxic dermatitis. Therefore, I should advise against the use of gold therapy. The tourniquet test

was in favor of a toxic process rather than discoid lupus erythematosus. There were none of the microscopic observations that go with a lupus erythematosus.

DR. DAVID BLOOM: Because of the presence of lesions on the hands I am inclined to consider this case as one of a subacute type of lupus erythematosus and not as a fixed type.

DR. E. WILLIAM ABRAMOWITZ: The patient has a fairly typical lupus erythematosus. The biopsy should be repeated. I think bismarsen should be administered if he has not had some already.

DR. MAURICE J. COSTELLO: I observed several cases of this type at Bellevue Hospital, and germanin was tried with some spectacular results after four or five injections. In only 1 patient did the administration have to be stopped because a toxic eruption developed.

DR. SAMUEL PECK: An important differential diagnostic point between disseminated lupus erythematosus and a chronic, rather widespread lupus erythematosus is the presence of capillary fragility in the former.

Pustular Psoriasis. Presented by DR. MAURICE J. COSTELLO.

E. C., a man aged 44, is presented from Bellevue Hospital. He states that the eruption began eight years ago, first appearing on the feet and three years later involving the palms.

The patient presents a symmetric eruption on the upper and lower extremities principally involving the palms and soles. There are several discrete lesions on the abdomen and back. The eruption consists of numerous pinhead-sized to pea-sized flattened pustules, each surrounded by a small halo of erythema.

When he was treated four years ago with superficial fractionated doses of roentgen rays and wet compresses the eruption disappeared for several months. At that time there was a bullous reaction to the intradermal injection of trichophytin. The urine and a complete blood count were normal. Culture of material from one of the pustules on the palm showed Staphylococcus aureus. Histologic examination showed an intraepidermic pustule. Recently his treatment has consisted of five attacks of fever produced with the inductotherm, with no benefit. He has received 35 Gm. of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) in the past two weeks. There has been a moderately favorable response to this therapy.

DISCUSSION

DR. DAVID BLOOM: This case is the second one of pustular psoriasis in which I have seen such an eruption on the legs. It is possible that the eruption on the palms and soles and that on the legs are identical in regard to nature and causation.

Necrobiosis Lipoidica. Presented by DR. FRED WISE.

M. F., a man aged 55, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 6, 1940 with cutaneous lesions of five years' duration. His father died of arteriosclerosis at the age of 74, and a brother died suddenly of heart disease. His youngest brother has diabetes.

The patient is 5 feet 4½ inches (164 cm.) in height, weighs 137 pounds (62 Kg.) and appears to be in good health. He has been having "indigestion" for many years and pain in the epigastrium for three years about five hours after meals, for which he has been taking sodium bicarbonate. He gives no history of jaundice or heart disease.

The lesions started on the dorsal surface of the middle of the great toe and at the insertion of the left achilles tendon as reddish pea-sized patches which gradually enlarged. They never showed any signs of regression. Two years ago similar patches appeared on the dorsal surfaces of the left second, third and fourth toes. He complained of some itching.

On the dorsal surface of the right great toe is a purplish red, fairly well marginated growth 1½ inches (4 cm.) in length, 1 inch (2.5 cm.) in width and 1 cm. in thickness. It is slightly raised and somewhat rough with an irregular border. The skin, the subcutaneous tissues and the tendon are firmly bound together but are freely movable over the bone. On diascopic pressure the color fades. There are similar lesions on the flexor surface of the right ankle, on the posterior surface of the left ankle and at the bases of the dorsal surfaces of the second, third and fourth left toes. A pea-sized nodule is also felt on the inner side of the middle of the left great toe. There are no other cutaneous lesions. The color of the skin of the feet is bluish, though he does not complain of intermittent claudication. The dorsalis pedis arteries are distinctly palpable.

The patient showed on several examinations 0.35 per cent of sugar in the urine. The hemogram and results of routine chemical examination of the blood were normal. The lesions examined under Wood's filter light did not show any fluorescence. Roentgen ray examination showed "no gross osseous or articular abnormalities of either ankle joint or foot." Chemical examination of the blood serum for lipids (according to the method of Bloor) taken on May 7, 1941 was as follows:

Total lipids	841 mg. per hundred cubic centimeters	(normal 500 to 700 mg.)
Fatty acids	571 mg. per hundred cubic centimeters	(normal 200 to 420 mg.)
Total cholesterol	170 mg. per hundred cubic centimeters	(normal 160 to 230 mg.)
Esters	170 mg. per hundred cubic centimeters	(normal 100 to 150 mg.)
Total esters	62 per cent	(normal 40 to 60 per cent)

A histologic report of a section taken on April 9, 1940 and examined by Drs. Satenstein and Sachs read as follows: "Possible necrobiosis lipoidica. Investigate for diabetes. Supply tissue to be stained for fat. Extending from the upper part of the cutis down to the bottom of the section there are large areas where the connective tissue has lost more or less its bundle structure and is more homogeneous. Around these areas there are a fair number of variously sized vessels. The walls in some of them are thickened, and around them there is a moderate amount of small round cells and connective tissue cells. The epidermis shows little of note."

A histologic section taken a week later, on April 16, was diagnosed as "granuloma annulare" by the aforementioned dermatopathologists, with the following description: "Throughout the cutis there are areas of connective tissue degeneration surrounded by epithelioid-like and small round cells. The vessels in part are dilated, and the walls in some of them are thickened. The epidermis shows nothing of note."

A histologic section taken on May 8, 1941 from the right ankle and examined by Dr. Sachs showed "necrobiosis lipoidica," with the following description: "The process is chiefly in the deep part of the cutis and fat. Throughout this zone there is considerable granular degeneration, and there is a diffuse cellular infiltration of connective tissue cells and some cells suggesting histiocytes. The vessels throughout the cutis are dilated, and about them is a focal cellular infiltration. In the deep portion the vessels are thickened, the intima is swollen and there is some breaking of the vessel walls. There are occasional giant cells. There is little or no change in the upper part of the cutis or epidermis. A slide stained with sudan III shows considerable fat in the deep part of the cutis."

The Schultz test did not show the characteristic brown and blue cholesterol crystals with blue edges (normally not found in necrobiosis lipoidica).

From April 23, 1940 till June 1 the lesions were treated with fractional doses of roentgen rays, a total of 2 units filtered through 1 mm. of aluminum (900 r) and ½ unit unfiltered (150 r). In November all the lesions were found to have undergone involution with the exception of a patch on the right leg. The patient

returned on April 25, 1941 with a recurrence of most of the growths. Another course of roentgen ray therapy was then given without any apparent benefit. A third biopsy was made on May 8, and a tentative diagnosis of necrobiosis lipoidica (diabeticorum?) was made. This diagnosis was corroborated later by the sudan III stain revealing fat droplets in the deep portion of the cutis. The urine, however, examined several times subsequently, failed to reveal any sugar, and the blood sugar, as already reported, was normal.

NOTE.—The patient was given a low fat and low cholesterol diet. He was seen about two weeks after this presentation. There was a decided regression of the lesions as a result of this dietary regimen.

Tinea Cruris (Trichophyton Purpureum). Presented by DR. GEORGE M. LEWIS.

M. H., a white man aged 34, is presented from the New York Hospital. An eruption developed in his right groin three years ago. This has been intensely pruritic and worse during the hot weather. His feet have periodically bothered him.

On examination there is a well circumscribed, erythematous, scaly and thickened, rounded plaque in the right groin. His feet show dull red, scaly soles with some interdigital maceration. There are lesions of tinea versicolor on the trunk.

Examination of specimens from the feet and from the lesion in the groin showed Trichophyton purpureum. There was a wheal-like reaction to trichophytin after fifteen minutes with no response after forty-eight hours or after one week.

Dermatitis Herpetiformis Controlled with Sulfathiazole. Presented by DR. MAURICE J. COSTELLO.

E. G., a white man aged 58, is presented from Bellevue Hospital. He states that he has had a generalized severe dermatitis herpetiformis (Duhring's disease), consisting of many grouped vesicles and bullae in addition to areas of depigmentation and hyperpigmentation and numerous excoriations, for the past seven years.

The urine and a complete blood count were normal. The Wassermann reaction of the blood was negative.

Previous treatment consisted of home remedies. Ten days ago he was given sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole), 4 Gm. a day. There has been decided relief of the intense pruritus, and all that remains of the eruption are the areas of hyperpigmentation. On one occasion since then administration of the drug was discontinued, with a recurrence of the pruritus and dermatosis and improvement when the sulfathiazole was again administered.

DISCUSSION

DR. ALBERT SCHUR: I had a duplicate case. That was before the advent of sulfathiazole. Four years ago I had a case of definite dermatitis herpetiformis of twenty years' duration. The patient was never free of the eruption. He was presented at many medical societies and never had any relief. I gave him sulfanilamide (that was before sulfapyridine), and he had a most miraculous result. His condition was cleared up completely within two weeks. I proved this result five times. When I stopped giving him sulfanilamide the eruption reappeared in forty-eight hours, and when he was given sulfanilamide again it disappeared. Now he is on a maintenance dose of 10 grains (0.65 Gm.) of sulfanilamide, and he is absolutely free of the eruption. In spite of the negative reports on the use of sulfanilamide in dermatology, this drug still needs to be considered one of the possible therapeutic agents.

BRONX DERMATOLOGICAL SOCIETY

LEO SPIEGEL, M.D., *President*

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April 24, 1941

Hypertrichosis Treated by Electrocoagulation. Presented by DR. CHARLES LERNER.

C. P., a woman aged 23, born in the United States, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has suffered from excessive growth of hair on the face for the past six years and on other parts of the body since childhood.

The patient is presented to show the result of treatment of hypertrichosis by electrocoagulation. The apparatus used is a small high frequency unit of the spark gap type, having a maximum capacity of 2 amperes and producing an oscillatory discharge which is highly damped and has a frequency of from 1,000,000 to 3,000,000 oscillations per second. The quantity of current being used on this patient is approximately 60 milliamperes. The technic is the same as that of ordinary electrolysis except that a foot switch is utilized to make and break the current. An average of forty to fifty hairs are removed in fifteen minutes.

Hypertrichosis Treated by Electrocoagulation. Presented by DR. CHARLES LERNER.

M. H., a woman aged 34, born in Russia, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, is suffering from hypertrichosis of the face. She has had twenty-three treatments, fourteen of which were by electrolysis and nine by electrocoagulation. She is presented to show the better results obtained with electrocoagulation. The technic and apparatus employed were the same as in case 1.

A Case for Diagnosis (Roentgen Ray Fibrosarcoma?). Presented by DR. CHARLES R. REIN.

Miss T. A., aged 52, states that in 1918 she received a series of weekly roentgen ray treatments for hypertrichosis. The treatments extended over a period of six months. In 1925 telangiectasia was noted. In 1924 keratoses had appeared on the cheeks. These were treated by electrodesiccation.

The patient presents telangiectasia, atrophy, pigmentation, depigmentation and dense sclerodermatous-like areas of infiltration along the sides of the face. There are pitted scars resulting from the electrodesiccation of the keratoses.

Histologic examination by Dr. Wilbert Sachs showed the entire cutis composed of a large mass of connective tissue fibers and cellular elements. The overlying epidermis was somewhat acanthotic, but there were no important changes. The connective tissue fibers were densely packed and ran in all directions. There was a diffuse cellular infiltrate composed chiefly of small and large spindle-shaped cells. There were some multinucleated cells and mitotic figures present. The histologic diagnosis was fibrosarcoma.

Roentgen Ray Anaplastic Epithelioma on the Floor of the Nose. Presented by DR. CHARLES R. REIN.

Miss B. S., aged 40, states that about twenty years ago she received a series of roentgen ray treatments for hypertrichosis. The treatments extended over a period of two and one-half years. Three years later the skin became dry and wrinkled. About ten weeks ago the patient noticed a small, painful, ulcerated

nodule in the right nostril. This gradually became larger and bled on the slightest irritation.

The patient presents telangiectasia, atrophy, pigmentation and depigmentation on the sides of the face, chin and lips. In addition, a hard, ulcerated painful nodule the size of a hazelnut is present on the floor of the right nostril and extends down to the right nasolabial fold. The edges of the ulcer are raised, rolled and pearly.

Histologic examination by Dr. Wilbert Sachs showed a large epithelial mass arranged in lobes, strands and bands near the bottom of the section at one edge. It was not connected with the epidermis. Throughout the cutis was a considerable small round cell infiltration. The cells composing the mass had large deeply stained oval nuclei. At one point there was some suggestion of whorl formations. The palisade layer was missing. The histologic examination showed anaplastic epithelioma.

On March 29, 1941 the lesion was removed by radical excision followed by facial plastic surgical repair with a sliding skin graft.

DISCUSSION OF REPORTS ON TREATMENT FOR HYPERTRICHOSIS

DR. ADOLPH ROSTENBERG: I have used electrocoagulation for the last twenty years. I believe that I was the first in New York city to advocate this method and published an article on its use (*M. J. & Rec.* **121**:751, 1925). There is no question in my mind that this method of removing hairs is far superior to electrolysis. It is speedier, as it takes only a few seconds for the removal of a hair, against one to two minutes by means of electrolysis; it is less painful and is not followed by scarring. I doubt, however, that more than seventy-five hairs can be removed in one sitting, as the field of operation becomes congested after half an hour or so and the patient cannot tolerate further treatment. The rate of recurrence in my experience is about 40 per cent, although it is difficult to distinguish between a recurrence and the appearance of new hairs. Owing to the unsatisfactory results of the galvanic method, the majority of dermatologists allowed patients with hypertrichosis to drift into the hands of the so-called electrolysis experts, which is to be regretted. I therefore urge that the electrocoagulation method be adopted by the dermatologist.

DR. PAUL GROSS: I wish to congratulate Dr. Lerner for popularizing the treatment of hypertrichosis by electrocoagulation. I have used this method since 1924, shortly after Bordier's first publication. Originally I used a mechanical interrupter, timing one tenth of a second, but soon found it more expedient to lengthen the exposure time and decrease the current. To measure the actual diathermy current with the patient in the circuit, I have been using a milliampere meter of the thermocouple type with a scale from 1 to 100 milliamperes, since the usual meter is not sensitive enough to register the small milliamperage of the electrocoagulation current used. I can subscribe to all the favorable statements made by Dr. Lerner, and observation over many years leaves no doubt in my mind that this technic gives excellent permanent results with most satisfactory cosmetic effect. This is due to the type of energy used and to the speed with which epilation can be performed. There is no comparison between the number of hairs removed by electrocoagulation and those removed by the galvanic current. Of importance also is the fact that owing to the shortness of the actual exposure one has all the necessary time for, and opportunity for relaxation in, the most essential act of the treatment, namely the proper introduction of the needle into the hair follicle. I am in disagreement with the conception that heat is formed only in an area extending from the needle point downward. The actual conditions show that heat is produced along the entire contact of the needle with the tissue and below, but with the current properly regulated the concentration of heat needed to produce coagulation can be localized around the needle point. Thus, surface coagulation can be prevented even without insulation of the needle, but special precaution is necessary for lanugo hair with its short root. It is well

to bear this fact in mind in gaging the current, despite the fact that no scarring ensues, even with a small degree of surface coagulation.

DR. SAMUEL PECK: I have been using bipolar electrocoagulation for epilation for years. The type of machine used is important in order to avoid scarring. It is my impression that the regrowth of hair is more frequent than with simple electrolysis. The advantage of the bipolar method, however, lies in the rapidity of the removal of hair. This in the last analysis counteracts any tendency for frequent regrowth.

DR. CHARLES WOLF: The electrocoagulation method has been extolled. There are, however, several points which require elucidation. Firstly, with regard to pain, it seems that more pain is caused by this method than by the galvanic current. Secondly, what percentage of hairs removed at each session recur? I feel that this method can be used with advantage in cases of extensive hypertrichosis, but in cases in which there is sparse hair the galvanic current should be used because of less pain and equally good results.

DR. CHARLES R. REIN: A machine of the type described by Dr. Lerner has been in use in my office for the past year. The pain is slight or at least no greater than with the galvanic type of machine. Recurrence varies from 10 to 25 per cent, but this depends more on the skill of the operator than on the type of machine used. I have found that the best results are obtained when the machine is set so that the hairs are destroyed in one to two seconds. If a longer time is required to destroy the hairs, one is more apt to obtain untoward sequelae. It is possible to remove about one hundred hairs in thirty minutes by this method.

DR. HENRY SILVER: I have treated a large number of patients with hypertrichosis over a period of years and never delegate the work to an assistant or technician. I have used both methods, electrolysis and electrocoagulation. My results were good, but I must immediately qualify this statement. I have never obtained a 100 per cent result and gave it up long ago as impossible to achieve. A 10 to 15 per cent regrowth should be expected. The treatment with electrolysis is painstaking, slow, painful at times but reliable. The galvanic current can be accurately measured, runs evenly and can be better controlled. Electrocoagulation is, however, the preferable method. With this method the technical skill is important. The method is time saving, and the number of hairs removed at one sitting is greater. Big machines are inappropriate; the smaller units give better results.

I am not in favor of chemical depilatories, pumice stone or peroxides. The ideal, of course, would be a permanent depilatory. About two years ago I became interested in the report of the explorer R. C. Gill, who carried out investigations in the jungles of Ecuador (*Natural Hist.* **41**:29 [Jan.] 1938). It dealt with the depilating qualities of a whitish root, Avelina blanca, which the native Indians from the Napo River use for removal of superfluous hair. Their skin, he stated, after one or two applications becomes smooth and shows no irritation and later no signs of atrophy and no regrowth of hair. Until such a depilatory is made available physicians will have to rely on hard-earned experience in treating hypertrichosis.

DR. FRANK C. COMBES (by invitation): I am acquainted with the article referred to by Dr. Silver. At the time of its publication I communicated with the Department of Agriculture and was informed that they were not acquainted with any plant or shrub known as Avelina blanca. Subsequently I wrote to the Pan American Horticultural Society in New Orleans. They were familiar with the story but said that the Indians who used it were unfriendly and that no one had succeeded in taking any of it out of the jungle.

DR. JONAS BORAK (by invitation): It is with reluctance that I discuss the roentgen ray treatment of hypertrichosis because the matter is so much disputed. Experience with the roentgen ray treatment of hypertrichosis should not be

separated from that acquired in the roentgen ray treatment of other diseases. The starting point of my method of treatment of hypertrichosis was my experience in the roentgen ray treatment of malignant tumors according to the method of Coutard. I saw surprisingly enough that patients with intraoral cancers treated by this method were permanently epilated and remained so after many years without any secondary changes in the skin. From this fact I drew the conclusion that this method might prove effective also in cases of hypertrichosis. My older method of treatment of hypertrichosis, as recommended by Holzknecht, was as follows: Four hundred r was given in one sitting. This was followed by a temporary epilation; after three months the treatment was repeated, usually six times. In most cases the epilation was permanent, but in many patients telangiectasia and atrophy of the skin developed.

Using the new method, only 125 r is given at a sitting. One application is given in the morning and another in the afternoon, for instance, at 9 a. m. and at 5 p. m. This is repeated daily until a total dose of 3,750 r is given. Two fields may be treated in one session. It may seem paradoxic that when the total dose is only 2,400 r given over one and one-half years the reaction of the skin is stronger than when 3,750 r is given in about three weeks. This is explained by the fact that constitutes the main principle of Coutard's method, namely, that small single doses are mostly accumulated by the hair follicles and less by the blood vessels and connective tissue. In addition, rays filtered through 0.25 mm. copper plus 1 mm. aluminum at 170 kilovolts are used. The dose is measured directly on the skin at each session. The results obtained this way prove that roentgen ray treatment of hypertrichosis is, to say the least, not so dangerous as is presented in textbooks.

DR. HENRY SILVER: Dr. Borak's contributions to dermatology in the field of roentgen ray therapy are well known. I have had the usual reluctance to employ roentgen rays in the treatment of hypertrichosis. Since listening to Dr. Borak's discussion, it is apparent that the more one knows the less one fears.

DR. CHARLES WOLF: I wish to comment on Dr. Borak's excellent discussion. My observations run along similar lines. About ten years ago, when high voltage treatment became the choice of treatment for carcinoma of the larynx, I noticed a permanent alopecia in the irradiated area of the neck and the lower part of the chin. Ten years has elapsed with many patients still under observation. Fortunately the internal cancers have been cured and the late effects of roentgen rays on the skin do not appear in these cases. The radiodermatitis is obviated by using heavy filtration, which removes the long waves which are most absorbed by the skin.

In reference to Dr. Rein's patient with radiodermatitis, showing fibrosarcoma, I have had occasion to observe her for the last fifteen years. From time to time there developed keratoses, which healed well when electrodesiccated. The usual sequela of radiodermatitis is prickle cell epithelioma. However, this patient has a fibrosarcoma, and this case is the first one of a sarcoma developing on the basis of radiodermatitis that I have encountered.

DR. HERMAN H. SAWICKY (by invitation): Both patients presented by Dr. Rein received roentgen ray therapy years ago for hypertrichosis. In 1 there developed an epithelioma at the floor of the nose, which has been treated by radical excision and plastic surgical repair. In the other patient there developed lesions on the side of the face, one of which was excised for microscopic examination and diagnosed as fibrosarcoma. This diagnosis, which was thought unusual, was corroborated by a number of pathologists.

DR. WILBERT SACHS: I am responsible for the diagnosis of fibrosarcoma in the case referred to by Dr. Sawicky.

DR. CHARLES LERNER: My two patients were treated by means of electrocoagulation. The advantage of this method is speed. A skilled operator can destroy approximately two hundred hairs per hour. I find less chance of scarring and pitting with this method than with electrolysis. It is not necessary to

employ an insulated needle, although its use tends to give the operator a greater sense of security. Pressure on the foot switch for about a second, repeated two or three times, is usually sufficient to destroy the papilla and the lower part of the follicle. One must, of course, be dextrous in entering the follicle and striking the papilla.

Lupus Erythematosus of the Face Associated with Psoriasis of the Legs Cured with Parenteral Liver Therapy. Presented by DR. PAUL GROSS.

E. C. M., a man aged 52, was shown at a meeting of the Section of Dermatology and Syphilis of the New York Academy of Medicine in January 1941 (ARCH. DERMAT. & SYPH. **44**:281 [Aug.] 1941).

The patient received twenty intramuscular injections of 5 cc. of liver extract daily followed by brewers' yeast every other day, 0.6 mg. of ferrous sulfate per day and five injections of iron adenylate. This treatment resulted in substantial clinical improvement of the lesions of lupus erythematous as well as of psoriasis. At present the skin of the face is clear but there is an erythematous scaly eruption on the vermilion border of the lips suggestive of lupus erythematosus. There has been no recurrence of the psoriasis.

DISCUSSION

DR. GIRSCH D. ASTRACHAN: I was interested in the fact that the patient presented a disturbance of the liver and that injections of liver extract favorably influenced the eruption. For some time I have been of the opinion that liver extract is useful for conditions associated with disturbance of the liver. On a former occasion I stated that erythema multiforme could be caused by a hepatic disturbance (enlargement of the liver with a rise in the icterus index) acting as a likely focus of infection. The injection of liver extract has been followed in my experience by improvement.

DR. LEO SPIEGEL: I saw this patient recently, and he is apparently cured of both cutaneous eruptions. He now complains of pains in the joints and there is swelling of the hands and knees.

A Case for Diagnosis (Horny Papules Under the Breasts). Presented by DR. SAMUEL FELDMAN.

M. S., a business woman aged 32, presented a generalized eczema on March 3, 1941. A week later it was casually noticed that the region under the breasts was studded with a large number of black papules. These were semiglobular, tough and horny. The follicular openings could not be made out, and the papules did not appear to represent horny plugs. When an attempt was made to remove one of these horny papules, a horny plate studded with papules came off. Later it was observed that a few follicular papules appeared in the axillas and here and there a tiny elevation capped by a black dot was seen to appear on the trunk.

Histologic examinations showed extreme parakeratosis. The horny layer was three times the thickness of the stratum germinativum. It had a wavy eppearance and gave the impression of darker and lighter tiers of reddish purple. The nuclei were retained in practically all the corneal cells. The granular layer was present in places and absent in others. The rete pegs were elongated. There were a mild edema of the cutis and a sparse infiltration about the blood vessels. The follicles were dilated. Some contained a horny plug, and from others the plug appeared to have fallen out. Dark stained homogeneous masses were seen in several locations either within a hair follicle or on the surface. These probably were foreign material.

DISCUSSION

DR. WILBERT SACHS: All the pigment is in the horny layer. The condition may be due to a fungus.

DR. SAMUEL PECK: The black color suggests to me an artefact, and the lesions do not impress me as being due to fungi. Cultures should be made.

DR. TIMOTHY J. RIORDAN (by invitation): The hostologic picture shows the nuclei split up into small granules and the granular layer gone. Some type of edema is present. There is an unusual type of parakeratosis. I was impressed by the clinical appearance of the lesion and thought it an artefact, but the keratosis makes one hesitate. In time the progress of the condition will clear the diagnosis.

DR. SAMUEL FELDMAN: It is of interest to note that ten days after the first visit I found these unusual lesions. The patient stated that they appeared in the last few days. It seemed rather strange that keratotic papules of that type would be of so short a duration, and it is likely that the patient and I overlooked the lesions. There were a large number of minute globular jet black papules covering the areas under the breast. They were in fact keratotic plaques, and I was able to pull off pieces of the keratotic skin together with four or more papules, indicating that these papules were not individual horny plugs with normal skin between them but were a part of a generalized keratosis. Microscopically the section presented a peculiar picture. Granular pigment was seen in the uppermost layers of the stratum squamosum. The clinical aspect is somewhat masked by the use of calamine lotion. Although there was much washing and scrubbing the material could not be removed. Black fungus is a possible cause.

A Case for Diagnosis (Pigmented Purpuric Lichenoid Dermatitis of Gougerot and Blum). Presented by DR. ARTHUR SAYER.

I. R., a white man aged 50, born in Poland, employed as a clerk in a stationery store, presented himself at the clinic of Mount Sinai Hospital in 1939, complaining of nervousness and indigestion.

The past history was unimportant, except that he was treated for exophthalmic goiter in 1913. No operation was performed, and he has been feeling fairly well for many years. Physical examination showed essentially no abnormalities except for a pulse rate of 108 per minute and hyperactive reflexes. Urinalysis showed no albumin or sugar. The basal metabolic rate was + 6 per cent. The Wassermann reaction was negative. The patient was referred to the clinic on account of an itching eruption of the feet, ankles and groins. He stated that this eruption has been present for about four years. He has not received any treatment for it.

The eruption on the feet differs from that in the groins. On the lower part of the abdomen and the adjacent parts of the thighs there are many discrete brownish and reddish papules, the size of a pinhead, which are not arranged in any pattern and show no tendency to coalesce. On the dorsa of the feet and around each ankle there is an extensive purplish eruption consisting of large plaques with wrinkled surfaces. Around the ankle there are numerous closely aggregated violaceous papules, dome shaped, not shiny, the size of a pinhead. The lesions do not extend to the legs. There is considerable itching at times.

DISCUSSION

DR. DAVID BLOOM: The lesions on the legs suggest lichen planus undergoing involution. As to the lesions in the groin, I should rely on the microscope to establish the diagnosis.

DR. SAMUEL PECK: I have had the opportunity of studying several cases of this kind. I do not believe that the condition in the case presented tonight can be designated pigmented purpuric lichenoid dermatitis, since there is no purpura and no telangiectasia. I suggest the diagnosis of lichen planus.

DR. FRANK E. CROSS: Lichen planus with an unusual distribution would be a likely diagnosis.

DR. ARTHUR SAYER: While it is difficult to establish a definite diagnosis, I am fairly certain that the eruption is not lichen planus. None of the lesions show characteristics that lichen planus ordinarily presents; none of the papules on the thighs or in the groins are flat, shiny or violaceous. If the skin is stretched the papules are definitely yellowish, with dome-shaped tops. Lesions from the groin and from the foot were excised for microscopic examination. The entire picture is unusual and does not seem to fit into any known classification. The diagnosis of pigmented purpuric lichenoid dermatitis is suggested because of the following characteristics: 1. Many of the elementary lesions are lichenoid papules. 2. Some of the lesions are purpuric. 3. Some pigmentation is seen interspersed between the papular lesions. In the description of the original cases of Gougerot and Blum mention is made of the presence of pinkish and brown papules, such as are seen in the groins in this case. The atrophy of the skin on the dorsa of the feet was not described in the cases of Gougerot and Blum.

NOTE.—Histologic examination showed the epidermis to be essentially normal. In the upper part of the cutis the blood vessels were moderately dilated and there was a sparse cellular infiltration around the blood vessels. There were no essential features on which a diagnosis of pigmented purpuric lichenoid dermatitis could be made.

Granulosis Rubra Nasi. Presented by DR. CHARLES PINES.

T. U., a schoolgirl aged 10 years, was seen at Bellevue Hospital on April 14, 1941. She presents an eruption on the nose which began about six years ago and has persisted, practically unchanged, to the present.

The skin covering the nose, especially the cartilaginous portion, shows areas of diffuse redness and well defined dark red macules and papules, the size of a pinpoint or pinhead. Interspersed among these lesions are droplets of perspiration. The nose is cold to the touch, and the affected skin is shiny and granular. There are a few minute papules on the cheeks and areas of telangiectasia on the upper lip. Subjective symptoms are absent, except for occasional itching and slight burning.

DISCUSSION

DR. LEO SPIEGEL: I presented a case of granulosis rubra nasi before this society in which the condition was much more pronounced than in the case presented this evening (ARCH. DERMAT. & SYPH. **39**:604 [March] 1939). The disease is most refractory to treatment. The condition in this case may be in an early stage, and continued observation should determine the diagnosis.

DR. ISIDORE M. LASHINSKY: I do not feel that the lesions on the upper lip fit into the picture of granulosis rubra nasi. These pinhead-sized lesions coupled with a history of nosebleeds suggest familial hereditary telangiectasia (Osler-Rendu).

DR. CHARLES PINES: The patient presents two of the most important features of the disease: (1) a persistent chronic dermatitis of the nose and (2) hyperhidrosis. Some observers report the disease as inherited by direct descent. In this case, however, there is no history that the disease has occurred in any other member of the family. The areas of telangiectasia on the upper lip are not unusual. The presence of telangiectasia has been reported in a number of cases of this disease.

Xeroderma Pigmentosum. Presented by DR. MAX BERKOVSKY.

E. G., aged 22, an American of Greek extraction, presents an eruption of eight years' duration. The younger brother has a similar condition.

The face and extremities are hyperpigmented. There are areas of atrophy and telangiectasia on the face. There are also some nodular lesions on the face. Several of these had been electrodesiccated with resultant scarring.

The patient does not have photophobia or lacrimation. The lesions are aggravated when exposed to the sun in the summer.

Histologic examination at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital corroborated the clinical diagnosis of xeroderma pigmentosum.

DISCUSSION

DR. CHARLES R. REIN: This patient had been under the care of my associate Dr. Frank, who destroyed many keratotic lesions by electrocoagulation. When we first saw him, his face was almost completely covered with keratoses. I can state that the patient shows about 75 per cent improvement.

DR. ARTHUR SAYER: An unusual feature is the absence of lesions on the dorsa of the hands. The other features, however, are characteristic enough to warrant the diagnosis of xeroderma pigmentosum.

DR. WILBERT SACHS: A lesion removed from the lip showed prickle cell epithelioma.

DR. FRANK E. CROSS: Two brothers are affected. It seems to me that this patient has a fairly good resistance to the disease. The average age at death of patients with this condition is about 20 to 21 years. He is 22, and the eruption is not far advanced. I also noticed the peculiar lack of pigmentation on the dorsa of the hands. Usually with this disease there is a history of consanguinity, which was absent in this case.

A Case for Diagnosis (Localized Myxedema). Presented by DR. CHARLES WOLF.

M. M., a girl aged 8 years, born in the United States, was in good health until the age of 4 years. At that time she was admitted to Morrisania City Hospital for bilateral swelling of the neck, which was diagnosed as cervical adenitis. While in the hospital enlargement of the spleen was disclosed on routine examination. The child had a normal birth. The parents and another child are living and well.

About one year ago an eruption appeared on the upper part of the legs and has gradually spread downward involving almost the entire anterior and somewhat the posterior aspects of the legs. The lesions consist of dusky, shiny red patches of irregular shape interspersed with narrow bands of normal skin. On palpation the lesions are infiltrated and yield on slight pressure.

The Wassermann reaction was negative. The cholesterol content of the blood was 228 mg. per hundred cubic centimeters. Examination of the blood showed 4,600,000 red blood cells, 80 per cent hemoglobin and 5,000 white blood cells, with 40 per cent polymorphonuclear leukocytes and 60 per cent lymphocytes. The basal metabolic rate in October 1940 was + 31 per cent. Histologic examination showed giant cells of the Langhans type in the deep layers of the cutis.

DISCUSSION

DR. SAMUEL PECK: I cannot agree with the diagnosis of localized myxedema. The atrophy plus the loss of subcutaneous fat suggest the diagnosis of acrodermatitis of an early type. One must concede the possibility of an endocrine cause in such cases.

DR. WILBERT SACHS: The patient has some type of fat disturbance. I would not make a diagnosis of xanthoma.

DR. DAVID BLOOM: Dr. Sachs's suggestion based on the histologic examination is well made and supports the clinical impression of some form of lipoid change in the skin, particularly in view of the presence of a large spleen. Hypercholesteremia is not a necessary feature. Further studies are necessary to clear the diagnosis.

DR. SAMUEL FELDMAN: In connection with this case, I recall a patient with acrodermatitis chronica atrophicans presented here a few years ago (ARCH.

DERMAT. & SYPH. **26**:1162 [Dec.] 1932), who showed xanthomatous nodules histologically. There may be a relation between lipoid disturbance and this condition.

DR. HENRY SILVER: I wish to correlate Dr. Sachs's histologic description and Dr. Peck's clinical impression. Dr. Sachs described some form of lipoidosis and Dr. Peck's clinical impression was that of definite atrophic change. This would suggest the form of lipoid disturbance described by Oppenheim as dermatitis atrophicans lipoidica.

DR. ARTHUR SAYER: I suggest the possibility that this child is suffering from Gaucher's disease. The age of the child, the large spleen and the lipoid disturbance seen microscopically suggest this diagnosis. The cutaneous condition may be a manifestation of Gaucher's disease.

DR. ABNER KURTIN (by invitation): During the discussion it has been stated that in exophthalmic goiter the cholesterol content of the blood is elevated; it is in myxedema that the cholesterol increases. On one determination the child had an increase in the basal metabolic rate. That is not sufficient evidence for a diagnosis of exophthalmic goiter, as all the other clinical signs are wanting. The clinical picture is that of a diffuse xanthomatosis. To clarify the diagnosis further, I suggest that roentgenograms of the bones be made, and if these are normal, a splenic puncture should be performed.

DR. CHARLES WOLF: My diagnosis was only provisional, and I appreciate the suggestions made. The important feature of the section studied is the presence of typical Langhans giant cells. A pathologist stated that the histologic picture was puzzling and that the numerous Langhans giant cells suggest leprosy.

Perforating Folliculitis of the Nose. Presented by DR. CHARLES R. REIN.

E. W., aged 30, was previously presented before this society in March 1941 (ARCH. DERMAT. & SYPH. **44**:969 [Nov.] 1941).

Histologic examination by Dr. Wilbert Sachs showed no evidence of epithelioma. There was a pronounced basophilic degeneration in the subepidermic region. The elastic tissue showed no abnormality.

CHICAGO DERMATOLOGICAL SOCIETY

LEONARD F. WEBER, *President*

MICHAEL H. EBERT, *Secretary*

May 21, 1941

Acanthosis Nigricans. Presented by DR. FRANCIS E. SENEAR.

J. A., a white girl aged 15, had been in good health except for being obese, weighing 187 pounds (85 Kg.) at the time of presentation. The cutaneous changes were first noticed about three years ago.

There are diffuse pigmentation and variable thickening of the skin on the back of the neck (extending inside the hair line), in the axillas, in the sternal region, under the breasts and on the folds of the abdomen, inguinal folds, external genitalia and perineum and folds of the knuckles. Aside from obesity and a mild hypothyroidism there were no pathologic observations on physical examination.

Examination of the blood (including chemical examination) and urine showed no abnormalities. The Wassermann reaction of the blood was positive. Roentgenographic studies of the gastrointestinal tract, skull and chest showed no pathologic changes.

Histologic examination of tissue from the chest showed the changes of acanthosis nigricans.

Acanthosis Nigricans (Juvenile Type). Presented by Dr. S. W. Becker and Dr. M. E. Obermayer.

J. M., a white girl aged 11 years, was seen one month ago complaining of dryness of the skin of the extremities and blackening of the skin of the axillas and neck for five years and intermittent diarrhea for eight years. There has been a gradual gain of about 40 pounds (18 Kg.) in weight during the past three years.

The patient was studied in the Bobs Roberts Memorial Hospital for Children (service of Dr. F. A. Schlutz).

The fat is distributed for the most part over the face, trunk and thighs. Her blood pressure was 140 systolic and 86 diastolic. There is some hypertrichosis of the lower part of the back. The skin shows hyperkeratotic and hyperpigmented rugae about the neck, axillas, genitalia and umbilicus. The skin in general is dry, and there are definite ichthyosiform hyperkeratoses on the dorsa of the hands and fingers.

A blood count showed 4,380,000 red cells and 7,400 white cells, with a normal differential count. There was 12 Gm. of hemoglobin per hundred cubic centimeters. The urine was normal. The basal metabolic rate was +2 per cent and —6 per cent on consecutive days. The reaction to a tuberculin test was negative. The result of a galactose tolerance test for liver function was normal. The dextrose tolerance test revealed decreased tolerance, as shown by the following blood sugar values: after fasting, 121.2 mg. per hundred cubic centimeters; one-half hour, 245 mg.; one hour, 383 mg.; two hours, 310 mg., and three hours, 242 mg. Chemical examination of the blood showed: nonprotein nitrogen, 26.6 mg. per hundred cubic centimeters; phosphorus, 3.72 mg.; calcium, 10.8 mg., and cholesterol, 114 mg.

Roentgenograms of the bones of the upper extremities showed no abnormalities of bony development. A pyelogram after intravenous injection of diodrast was normal.

The histologic examination showed the usual picture of acanthosis nigricans. The dopa reaction revealed dendritic dopa-positive melanoblasts distributed at intervals along the epidermodermal junction.

DISCUSSION OF TWO CASES OF ACANTHOSIS NIGRICANS

Dr. Udo Wile, Ann Arbor, Mich.: It is an unusual opportunity to observe 2 such cases at one time. There was reported many years ago from my clinic a case which was similar to the first case presented. The question was raised at that time as to whether the condition has the same clinical significance in children as in adults, since in the former it is frequently associated with malignant disease. It was said at that time that the only yardstick would be the measure of time itself. It so happened that in the last two years I had a letter from the young girl presented with juvenile acanthosis nigricans when she was 14. She is now married and has children. She is progressively getting darker but is in good health. It seems to me that one must differentiate sharply between the cases in which the disease comes on late in life and has a relation to malignant neoplasm and these cases in which it occurs in children. Clinically, I do not think there is the slightest difference between them, that is, the cases that carry a serious prognosis and the ones that do not. There is no way of differentiating them.

Dr. S. W. Becker: The only abnormalities that we can find in our patient are the rather peculiar obesity, which is not unusual in such children, and the rather pronounced decrease in sugar tolerance. She has not had a roentgenogram of the skull to determine the size of the sella turcica. Acanthosis nigricans is really a misnomer. The condition is a papillary overgrowth with little acanthosis. I have a section from this girl's lesion, prepared by the dopa method, which shows a rather mild pigmentary activity.

I agree with Dr. Wile that there is no method of differentiating between the so-called congenital and malignant varieties. Occasionally the malignant variety is seen in a fairly young person; so one must be rather cautious. This child has been examined carefully, and no sign of malignancy can be elicited at present.

Favus. Presented by DR. S. J. ZAKON (by invitation) and DR. T. BENEDEK (by invitation).

I. M. F., a Jewish girl aged 9 years, born in Chicago, presents an eruption of the scalp of nine years' duration.

Examination shows the presence of favus scutula on the scalp and areas of alopecia with atrophy. There is no familial history. The child is at present living in an orphanage.

Histologic examination of the hairs and crusts showed favus. Cultures of Achorion schoenleinii were demonstrated. Examination with wood-filtered ultraviolet radiation showed fluorescent hair throughout the scalp and involvement of the skin of the forehead, eyelids and ears.

DISCUSSION

DR. JAMES H. MITCHELL: This case is a classic one. Some years ago I demonstrated an American-born mother and 2 children and another American-born mother and her daughter (ARCH. DERMAT. & SYPH. **24**:694 [Oct.] 1931). In the one group there was a history of favus in three generations and in the other in four generations. I was interested in this child because she had been living in an orphans' home for a year and had had the disease for nine years. She said that her mother was not similarly affected.

DR. MINNIE PERLSTEIN: I know the mother and knew the father, who is now dead, and neither of them had any diseases of the scalp. The girl has an older brother, who is well. She was not isolated from other children until last year when she was taken to the orphans' home. No one with whom she was in contact had the condition.

DR. MICHAEL H. EBERT: Did she have treatment?

DR. MINNIE PERLSTEIN: No.

Papulonecrotic Tuberculid. Presented by DR. FRANCIS E. SENEAR and DR. MARCUS R. CARO.

G. B., a white woman aged 23, sustained an injury to the left breast in 1938. This was followed by pain and a purulent discharge at the site of the injury. Healing occurred, but a draining sinus appeared to the right of the nipple in September 1939. The following month the inflammatory mass was excised, and a histologic examination of the tissue showed "a histiocytic response suggestive of tuberculosis."

About one month after the operation lesions appeared on the face, and these have continued to appear since then. Roentgenographic examination of the chest at that time was "negative for active or recent pathologic changes."

The patient presents discrete, hownish yellow, pea-sized lesions on the forehead, along the hair line and on the sides of the neck. These lesions are firmer than the surrounding skin and globular, and some are slightly umbilicated in the center, but there is no clinical appearance of necrosis or sloughing. Pressure with glass shows a residual apple jelly nodule at the site of a lesion. In addition there are several lesions of acne vulgaris on the face.

Histologic examination of tissue from the forehead showed a dermal papule. The epidermis was flattened and contained considerable intracellular edema. In the corium there was a circumscribed mass of infiltration which extended throughout the entire depth of the corium. In this mass there were small areas of necrosis and several foci of giant cells and epithelioid cells surrounded by a densely packed mantle of lymphocytes. This infiltrate extended up to the epidermis, which in one place showed complete dissolution. Acid-fast bacilli were not found.

DISCUSSION

DR. FRANCIS E. SENEAR: This case was presented as one of micronodular tuberculosis, with a bow to Dr. Michelson, since so often there is disagreement

as to the proper designation of conditions of this type. I think it is advisable to call this condition acnitis or miliary lupus on the basis of the clinical observations. Dr. Caro thought it should be diagnosed acnitis rather than miliary tuberculosis from the histologic observations.

Urticaria Pigmentosa. Presented by DR. A. W. STILLIANS and DR. E. M. SMITH JR. (by invitation).

When the patient, a white girl, aged 2 years and 9 months, was 4 months old, pink spots appeared first on the back, neck, scalp, trunk and extremities and lastly on the face. The spreading was gradual over a period of several months. Itching developed with an attack of hives at 9 months of age. Constipation has always made the hives worse. Formation of vesicles has not been extensive, and there are few on the extremities and face. The patient tends to improve on a normal diet. Pigmentation has remained about the same. One cousin and one aunt are allergic (asthma and hay fever respectively).

Examination shows patches of pigmentation over most of the body. Dermographism with some wheal formation is present. There are tiny vesicles on some of the pigmented areas.

The mother stated that the treatment had included special allergy diets, ultraviolet irradiation (which only increased the pigmentation) and the administration of thyroid, vitamins, histaminase and calcium tablets, with no results.

Examination of the blood revealed 5,360,000 erythrocytes, 76 per cent hemoglobin and 17,350 leukocytes, with 3 per cent neutrophils, "band" forms, 51 per cent segmented forms, 38 per cent lymphocytes, 1 per cent eosinophils, 2 per cent basophils and 5 per cent monocytes.

Urticaria Pigmentosa. Presented by DR. N. C. BARWASSER (by invitation), Moline, Ill.

R. S., a white woman aged 29, states that the lesion has been present for about five years, beginning on the arms and chest and spreading over the entire body in about a year.

The past and family histories are irrelevant.

The eruption consists of discrete, copper-colored macules, varying in size from that of a pinhead to that of a split pea. They are present on all parts of the body with the exception of the palms and soles. The pigmentation appears to be deeper after bathing and during the summer.

The Kahn reaction was negative. Scrapings from the lesions revealed no fungi. The reaction to a Darier test was positive.

DISCUSSION OF TWO CASES OF URTICARIA PIGMENTOSA

DR. OTTO FOERSTER, Milwaukee: These cases are interesting instances of the disease. In Dr. Stillians' case there are clinical features which could lead to confusion with xanthoma. I recall that years ago Dr. Pusey pointed out this close resemblance in some cases. The urticarial feature in Dr. Stillians' case was unusually prominent.

DR. S. W. BECKER: The division of the disease into congenital and acquired types is not justified, because about 50 per cent of the eruptions will appear during the first six months and from then on there will be a gradual tapering off of the frequency of onset. It is not logical to divide the disease into two distinct varieties.

DR. CLARK W. FINNERUD: The case presented by Dr. Smith was interesting because in so few instances are there vesicular lesions. In the group of 308 cases I summarized in 1923 (ARCH. DERMAT. & SYPH. **8**:344-358 [Sept.] 1923), including those of Little, in 5.5 per cent the disease was characterized by vesicular or bullous lesions. So far as the acquired type is concerned, since 1905 in something like 24 per cent of the cases the disease appeared after the age of puberty.

A Case for Diagnosis (Pseudopelade or Lupus Erythematosus). Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

E. S., a man aged 30, noted a spot of alopecia on the left temporal region about five years ago. In succeeding years the other areas of alopecia have appeared. Confluence of some lesions has taken place. There have been no remissions at any time. He had been treated by means of injections of gold salts.

Examination reveals ivory-colored atrophic patches of alopecia all over the scalp, some of which are confluent. There is plugging of the follicles in some places.

The Kolmer and Kahn reactions of the blood serum were negative, and the urine was normal.

Histologic examination of a section of the scalp showed moderate hyperkeratosis with plugging of a prominent indentation, which, however, was not seen to be intimately associated with a hair follicle. The epidermis was thinned, with only a few rete processes. Both superficially and deep in the cutis there were irregular areas of fibrosis. No hair follicles or sweat glands could be seen, although arrectores pilorum were present in four places.

DISCUSSION

DR. CLARK W. FINNERUD: I think the condition is pseudopelade.

DR. DAVID V. OMENS: The patient said I saw him about five or six years ago and that I then made a diagnosis of lupus erythematosus. However, I do not remember the case.

DR. MARCUS R. CARO: It seemed to me that in one of the areas on the vertex there was a distinct folliculitis.

DR. S. W. BECKER: When I first saw the man the presence of the plugged follicles led me to consider a diagnosis of lupus erythematosus, but the section does not verify the diagnosis. It shows superficial and deep fibrosis of a type which is not present in lupus erythematosus but is present in pseudopelade. The ivory-like color of the plaques favors the diagnosis of pseudopelade. This patient was seen at the Mayo Clinic, where the diagnosis was pseudopelade. He was seen by several dermatologists in Chicago and New York, among them Dr. Omens. He was given gold therapy by one or two other physicians; so I presume they made a diagnosis of lupus erythematosus.

Lupus Erythematosus. Presented by DR. I. M. FELSHER (by invitation) and DR. IRENE NEUHAUSER (by invitation).

A. W., a white man aged 63, born in Poland, a gasoline station attendant, was admitted to the Mandel Clinic of Michael Reese Hospital on May 3, 1941, complaining of an itching eruption that had begun in January 1940.

He stated that he always had a "ruddy face" but that it turned a deeper red and became swollen at the time of the onset of the attack. The eruption, with itching and scaling, spread rapidly to his neck, ears and scalp. Within a few months the lesion in these areas became less acute and a similar eruption appeared on his arms and hands. A few months later the legs bore the brunt of the attack, and finally, within the last three or four months, the lesions on the trunk appeared. He enjoyed good health until this eruption appeared, and his chief complaint since then has been severe itching.

On examination he presents erythematous areas on his face interspersed with areas of brown pigmentation and atrophy and telangiectasia. Similar erythematous patches with atrophic areas and deeper red scaling papules are present on the neck, ears and scalp. On the sternal area, abdomen, upper part of the back and lumbar and sacral areas there are patches of more vivid red, covered with gray scales, and in the periphery of these patches there are isolated or grouped scaling papules as well as atrophic areas. On his arms there are patches of light red

scaling papules with atrophic areas and patches of diffuse erythema that change to a livid or purplish red, particularly on the dorsa of the hands. On his legs there are also patches of livid red with thickening of the skin dotted with excoriations and a few scattered scaling papules. The lesions on the legs end sharply at the level of the tops of his shoes. The feet are bluish red.

The significant observations in the physical examination are a systolic blood pressure of 200 and a diastolic of 110 and a temperature of 99.6 F.

Examination of the blood showed no abnormalities. Urinalysis revealed a slight reaction for albumin and 2 granular casts with occasional leukocytes and erythrocytes per high power field. The Wassermann and Kahn reactions of the blood were negative. A roentgenogram of the chest showed the cardiac-thoracic ratio within normal limits, the hilar and general pulmonary markings increased bilaterally, the costophrenic angle blunted on the right and an old pleural thickening with probable calcification in the left apex.

Histologic examination of tissue from the right side of the chest showed a picture consistent with lupus erythematosus.

DISCUSSION

DR. MICHAEL H. EBERT: There are some interesting features about this case from the clinical point of view. On the patient's lips there is a faint pearly discoloration which could be associated with lupus erythematosus or lichen planus. On the face and neck on each side there are areas where one can make out definitely flat shiny papules, and one could imagine whitish lines in some of them. In addition the patient complains of intense itching. That suggests lichen planus. Against the diagnosis of lichen planus there is this peculiar distribution of the lesions on the face and scalp. He says the condition started in the scalp. In favor of lichen planus are the lesions on the lips. Other facts are his sex and age. Acute disseminated lichen planus invariably occurs in women. In the vast majority of cases the subacute type occurs in the female, and to that exception this type would in itself be unusual. In the histologic section there was a destruction of the elastic tissue, but one must consider the age of the patient.

I could not make a diagnosis of lupus erythematosus from the section. I do not believe there is enough degeneration of the basal layer. While there was some infiltrate one could not be certain that the disease was lupus erythematosus. I still think it is lichen planus. In several cases presented before this society there were lesions on the mucous membrane and vermilion border of the lips and on the body, and the discussion always favored lupus erythematosus. Dr. Finnerud has pronounced a dictum that if the face is involved this type of eruption is lupus erythematosus. That would argue against my statements.

DR. MARCUS R. CARO: About eight years ago I presented a similar case with the diagnosis of lichen planus (ARCH. DERMAT. & SYPH. **29**:477 [March] 1934). Dr. Finnerud in the discussion said that in a case in which lupus erythematosus and lichen planus could not be differentiated readily and the histologic picture was not clearly diagnostic, the case would usually turn out to be one of lupus erythematosus. The further course of that patient showed the diagnosis of lupus erythematosus to be correct. I believe that in the present case the diagnosis of lupus erythematosus can be established both clinically and histologically.

Sickle Cell Anemia with Ulcer. Presented by DR. FRANCIS E. SENEAR and DR. THEODORE CORNBLEET.

This 17 year old boy has been under observation for thirteen years because of anemia. Two to three months ago an ulcer developed on his leg.

DISCUSSION

DR. FRANCIS E. SENEAR: This case was presented to show the ulcer associated with this type of anemia. I think it is of interest that the patient had

been under observation for thirteen of his seventeen years and the ulcer developed while he was under observation.

A Case for Diagnosis (Alopecia Areata of the Scalp and Eyebrows and Psoriasis of the Nails or Paronychia Congenita?). Presented by DR. EDWARD A. OLIVER and DR. CLEVELAND WHITE.

G. L., a boy aged 10 years, observed at the dermatologic department of Northwestern University Medical School, presented no abnormalities at birth. When he was 3 years old a scaling occurred on the nail of the right index finger. The nail of the left index finger and the corresponding nails of the right and left hands were later involved. All the toe nails were involved within six months. No pain or inflammation was present. The patient was first seen six years ago and again recently.

The proximal third of each finger nail is pink, and the distal two thirds is opaque, thin, discolored, brittle and linear. A depression is present to the distal third of the nail. The proximal ends of the nails of the big toes are convex, and the distal ends are depressed and do not reach over the distal end of the toes.

About three years ago a loss of scalp hair followed an accident and the lesions have increased in size and number. There is a partial loss of the lateral third of the eyebrows of recent origin.

His weight has increased 10 pounds (4.5 Kg.) within the past six months. The results of laboratory examinations have been repeatedly normal.

DISCUSSION

DR. A. W. STILLIANS: I have repeatedly seen involvement of the nails with alopecia areata. This involvement developed early, and the alopecia areata appeared much later.

DR. CLARK W. FINNERUD: I thought the condition was alopecia areata, rather than psoriasis, with associated dystrophic changes in the nails.

DR. MINNIE PERLSTEIN: During the past two years I have seen 2 patients with the combination of alopecia areata and dystrophy of the nails, one a university student aged 18 and the other a housewife aged 25. The changes in the nails appeared during one month. I gave both the patients vitamin B complex, and in about seven months both conditions cleared up in each of them.

DR. CLEVELAND WHITE: This patient has had the dystrophy of the nails for eight years but the alopecia areata for only a few months. Psoriasis was the diagnosis made for this boy last fall. He has had a great deal of vitamin therapy, especially vitamins A and B. I think the condition is alopecia areata with dystrophy of the nails. The dystrophy of the nails came on a long time before the alopecia areata.

A Case for Diagnosis (Mycosis Fungoides?). Presented by DR. FRANCIS E. SENEAR and DR. HENRY C. SCHORR (by invitation).

F. L., a white man aged 57, presents several sharply circumscribed, erythematous and slightly scaly patches on the arms and legs. These lesions have persisted for about two years and have caused much itching at times.

The blood was normal. The administration of 1 grain (0.065 Gm.) of phenolphthalein was not followed by an exacerbation of the lesions.

Histologic examination of tissue from the arm showed slight acanthosis and edema of the epidermis. In the upper part of the corium there were small circumscribed foci of infiltration about the blood vessels, and these were composed largely of lymphocytes. The infiltration was especially dense in several papillae.

DISCUSSION

DR. M. R. CARO: Histologically it was impossible to make a definite diagnosis of mycosis fungoides. There was a good deal of infiltration in the upper

part of the corium composed of different types of cells, but these observations were not diagnostic.

DR. UDO WILE, Ann Arbor, Mich.: I think it should be reemphasized that mycosis fungoides is a clinical and not a microscopic diagnosis. The microscopic picture in a typical clinical case may vary greatly; the infiltrate may be of the so-called polymorphous type or of any cellular type, such as occurs in lymphosarcoma or Hodgkin's disease, or, as in 1 case recorded by myself, the infiltrate may be an eosinophilic one. If this is true, it is not proper to say that the histologic picture is typical of mycosis fungoides, since that diagnosis is purely a clinical one.

DR. FRANCIS E. SENEAR: The patient's condition was a puzzle to us. We simply presented him with the thought that he might show clinical changes of mycosis fungoides.

Papulonecrotic Tuberculid. Presented by DR. EDWARD A. OLIVER and DR. IRVING A. LEWE (by invitation).

E. F., a white man aged 62, was first seen at the clinic of Northwestern University Medical School on March 19, 1941. He stated that his present trouble started about two months before and was first manifested by a swelling in the right inguinal region which rapidly became fluctuant and drained pus for several days. About the same time an asymptomatic eruption appeared on the lower parts of the legs and gradually spread to involve the entire surface of both lower extremities and the buttocks, with a few scattered lesions on the back and lower part of the abdomen. There was no personal or family history of tuberculosis.

The patient presented an indurated mass in the right inguinal region with healed linear scars along the inguinal groove. The eruption covered the described areas in a symmetric fashion. The individual lesions were discrete, and varied from reddish papules, most of which had hemorrhagic and crusted centers, to older round macular and maculopapular lesions with scar formation.

Treatment has consisted of three weekly injections of neoarsphenamine (0.15 Gm.). The patient now shows striking improvement. All the lesions are clearing. Some have almost completely disappeared, and others are marked by round depressed white atrophic scars with a surrounding zone of brownish pigmentation.

The Frei test with two different antigens elicited negative reactions. The reaction to a Vollmer tuberculin patch test was positive. The Kahn reaction was negative. The urine and blood count were normal. Roentgenographic examination of the chest showed no evidence of tuberculosis.

Biopsy specimens were taken from a primary lesion and two older lesions. The epidermis of the primary lesion showed a moderate amount of intracellular edema but was otherwise normal. Occupying the center of the corium was a well circumscribed oval mass of dense cellular infiltration. The upper third of this mass was composed almost entirely of polymorphonuclear leukocytes, and the lower portion consisted of a central zone of epithelioid cells, fibroblasts and several Langhans giant cells, with a peripheral zone of small lymphocytes. The diagnosis was papulonecrotic tuberculid. A section of an older lesion presented a moderate perivascular infiltration of young fibroblasts and a few small lymphocytes in the upper part of the corium. There was no tuberculoid infiltration. In another section of an old lesion the epidermis showed irregular acanthosis. In the center of the section was an erosion of the epidermis filled with exudate. The upper part of the corium presented a moderate perivascular infiltration of young fibroblasts, with a few small lymphocytes and polymorphonuclear leukocytes. There was no tuberculoid infiltration.

DISCUSSION

DR. FRANCIS E. SENEAR: I felt that the condition in this case was an example of this disease. I wanted to speak of a case Dr. Michelson and Dr. Caro presented (report not published) at the meeting of the American Academy of

Dermatology and Syphilology in December 1940. A young woman with crops of lesions on the extremities had been under observation for fifteen years. She was looked over repeatedly for evidence of tuberculosis with nothing discernible. During the past year she was a patient in the department of gynecology and was found to have an abdominal mass. She was operated on two months ago, and such a pronounced tuberculous infiltrate was found around the tubes that it could not be removed. It is interesting that one could observe the cutaneous lesions for so long with no demonstrable visceral lesion.

DR. OLIVER S. ORMSBY: Before the subject of tuberculid was well worked out there were two independent conditions termed folliclis and acnitis. T. C. Fox grouped these together as papulonecrotic tuberculids. The lesions of folliclis usually were grouped and situated on the extremities. Those of acnitis occurred on the face and were discrete papulopustules which crusted and underwent involution, leaving scars. The old term folliclis would fit the condition in the present case.

Acrosclerosis. Presented by DR. MICHAEL H. EBERT.

R. G., a white man aged 58, maintains he has been in good health until one year ago, when he first noticed coldness and blueness of his hands and feet with stiffness of the fingers on exposure to cool water or air. He consulted physicians and was told he had Raynaud's disease, for which surgical therapy was recommended. This he refused. About two months ago he noticed increased pain in the extremities and a "binding down" of the tissues of his hands and feet. Numbness and tingling of the extremities have since appeared. The essential feature in the patient's past history is a thyroidectomy performed in 1935.

On physical examination one notes the firm adherence of the tissues of the hands, forearms, feet and legs to the underlying structures. On the chest and back are many flat, dime-sized, smooth, shining, firm plaques.

The urine and the blood count were normal. Chemical examination of the blood showed nonprotein nitrogen 45 mg., creatinine 1.6 mg., calcium 9.3 mg., phosphorus 5 mg. and phosphatase 24.4 mg. (uormal 1.5 to 4 mg.) per hundred cubic centimeters. The Wassermann reaction was negative, and the basal metabolic rate —5 per cent. Roentgen ray study of the hands and feet showed normal bone structure. The histologic picture was compatible with the diagnosis.

DISCUSSION

DR. M. E. OBERMAYER: I think the condition in this case is a good example of acrosclerosis. I should like to point out that treatment with raw pancreas, a form of therapy elaborated by Sellei in Budapest, is not beneficial in acrosclerosis but gives fairly satisfactory results in ordinary scleroderma. This observation adds perhaps to the concept that the two disorders are distinct entities.

DR. OLIVER S. ORMSBY: The patient has what is called diffuse scleroderma in this country. At the International Congress in Budapest Sellei showed a group of patients with scleroderma and sclerodactylia, and he termed their disease acrosclerosis. He stated that in true scleroderma the sclerosis spreads downward from the arm over the hand and fingers, while in acrosclerosis the reverse direction of progress occurs. He gave a large number of points of distinction between the two conditions. Most of the Americans considered his cases as instances of diffuse scleroderma. Dr. O'Leary was of the opinion that acrosclerosis should be distinguished from diffuse scleroderma. It will be necessary to study these cases much further to determine whether the condition should be considered distinct from scleroderma. I think the present patient presents typical diffuse scleroderma.

DR. MAURICE OPPENHEIM (by invitation): I think Dr. Ormsby is right. It is known that scleroderma can start on the fingers and hands. It is called sclerodactylia. This condition is often combined with scleroderma of the body. Often

scleroderma starts on the face and breasts. It is not so often that it starts on the hands and fingers, from where is ascends. In Budapest acrosclerosis (Lettei) is separated from scleroderma. Dr. Ormsby may be right that such cases should be observed to see if acrosclerosis and scleroderma are different diseases.

DR. MORRIS WAISMAN (by invitation): I agree with Dr. Ormsby that this case is not an instance of acrosclerosis, but I believe that there are conditions which correspond to this partial type of vasomotor scleroderma. Last year Dr. O'Leary and I reviewed 64 cases of acrosclerosis (*Proc. Staff Meet., Mayo Clin.* **15**:702-704, 1940; Collected Papers of the Mayo Clinic and the Mayo Foundation, Philadelphia, W. B. Saunders Company, 1940, vol. 32, pp. 758-761) and concluded that the condition is a distinctive entity. The syndrome combines Raynaud's phenomena with secondary scleroderma of the distal parts of the extremities and of the face, the neck and sometimes the upper part of the chest. As Sellei has pointed out, the skin is taut rather than actually hard. The face becomes drawn and stretched; the fingers appear stiff, semiflexed, bulbous or tapering; the finger tips show dystrophic changes, and the nails are deformed and stunted. Early symptoms of acrosclerosis are those due to intermittent arteriolar spasm in the hands, and sclerodactylia occurs simultaneously with the vasomotor symptoms or at a variable interval afterward. Like Raynaud's disease, acrosclerosis is seen chiefly in women. Men are relatively infrequently affected, and that is one reason why the diagnosis presented for this case may be questioned. We found that in approximately 10 per cent of cases of Raynaud's "disease" the fingers and sometimes the hands are involved secondarily by sclerodermic changes, thereby constituting a mild and often unrecognized form of acrosclerosis. The prognosis in cases of acrosclerosis is generally favorable, as often material improvement occurs either spontaneously or as a result of treatment.

For the diagnosis of acrosclerosis the vasomotor symptoms are most important, consisting of a typical triphasic succession of color changes in the fingers. It must be remembered that many other unrelated vascular diseases often exhibit symptoms similar to those of Raynaud's disease during their clinical course. Also, in some cases of scleroderma such symptoms follow the appearance of sclerosis, owing to the vascular obliterative changes present. One must especially differentiate diffuse scleroderma in which the onset is associated with Raynaud's phenomena and in which sclerosis occurs first over the acral parts but extends ultimately over wide regions of the body, often becoming generalized. Dr. O'Leary and I observed that this form affects the two sexes equally and, moreover, that it invariably attains great proportions within two years after the onset, as distinguished from acrosclerosis, which retains its restricted distribution. I think the condition in the case presented by Dr. Ebert belongs to this variety of scleroderma, a form better termed progressive diffuse scleroderma. The prognosis of the latter condition is unfavorable, in contrast to that of acrosclerosis. Histopathologically there is no difference between acrosclerosis and generalized scleroderma, and this is true not only of the skin but of the skeletal musculature as well, which we found characteristically involved in all patients examined.

DR. J. E. GINSBERG: I do not think it was mentioned in the history that this man has depigmented lesions on the neck and chest, which, I believe, are related to the whole disease picture.

DR. MICHAEL H. EBERT: The purpose in presenting this case as one of acrosclerosis was to stimulate discussion as to what acrosclerosis really is. From the little I have read of it and what little experience I have had, I should have thought frankly that this condition today would fit into the category of acrosclerosis. It started as a Raynaud's syndrome, and there was a definite history of blanching and then reddening and vasomotor disturbances of the fingers of the type called Raynaud's disease. On testing, the peripheral vessels were found to be patent. The other feature mentioned by Dr. Ginsberg, pigmentary changes and hyperpigmentation on the chest and back, is characteristic of generalized scleroderma. There was one finding in the laboratory examination that was not normal.

The phosphatase content of the serum was extremely high. That would indicate some disturbance of calcium metabolism. I believe it is in the type of condition that used to be called sclerodactylia that there is a withdrawal of calcium from the bones and a deposition in the skin, eventually sloughing out. This phenomenon has not occurred in this case. The bones are still normal. A serum phosphatase content of such high degree would indicate that there is a tendency to mobilization of calcium. Whether thyroidectomy which preceded the onset of this disease by two years had anything to do with the disease is a question. In discussions on the causation of scleroderma one always comes back to the statement that thyroid involvement is sometimes present.

Dermatitis Exfoliativa (Type?). Presented by Dr. Clark W. Finnerud and Dr. Ralph B. Coomber (by invitation).

L. K., a man aged 28, ten years ago noticed an eruption of water blisters and pustules on the trunk and extremities, which cleared in several months. One year later he noticed an itching and scaling patch on the left forearm, which rapidly spread to involve the surface of the entire body as a diffuse, bright red, scaling eruption. The patient was continually cold except in the very warmest weather. Seven years ago he received approximately two dozen roentgen ray treatments to most of the areas, after which the eruption cleared for a short time but then recurred. Three years ago the eruption again disappeared after the administration of internal medicine but again recurred after a short interval.

The patient was an outstanding athlete in high school and college, and two years before the advent of his original eruption he was "spiked" in a track meet and was given an antitetanus injection. There is no history of any previous eruption. On premarital examination one year ago the Wassermann reaction was found to be positive, and he was given intravenous injections. But after five such injections his hands swelled so greatly that intravenous treatment was discontinued. He was then given a series of injections of bismarsen.

Examination discloses a well developed man with a generalized erythema associated with exfoliation of heavy scales of universal distribution. Apparently the knuckles are the only areas which show no involvement. There are dystrophic changes of the finger nails which cannot be said to be psoriasiform in type.

The blood was normal. The Wassermann and the Kahn reaction were 4 plus.

Histologic sections showed typical epidermal and dermal changes characteristic of psoriasis aside from the absence of the so-called Monro abscesses.

DISCUSSION

Dr. Francis E. Senear: I think it is impossible in a case of exfoliative dermatitis of this type to do any more than speculate on the things that may give rise to complete exfoliation. Pityriasis rubra pilaris has to be considered here on the basis of experience with 2 cases observed with Dr. Pusey. The striking symmetry would suggest the picture of this disease.

Dr. Oliver S. Ormsby: Dr. Senear's suggestion of a possible pityriasis rubra pilaris is an excellent one, and I agree with his statements concerning the consideration of several possible conditions when one is studying generalized exfoliative dermatitis. In this case I believe the erythroderma of lymphoblastoma can be ruled out. In view of the patient's history, that he had an early scaly eruption which was successfully treated with roentgen rays, it is possible that this condition might have been psoriasis which, on recurring, developed into a general exfoliative dermatitis either through a normal evolution or from medication (arsenic). Such a transition is not uncommon. The erythroderma of lymphoblastoma is sufficiently characteristic so that one can frequently make a diagnosis before changes in the blood have occurred. Several patients like this one have been shown before this society. I have a striking case at present, which was first observed in January. This was one of generalized exfoliative dermatitis with a normal blood picture.

Since that time general adenopathy has occurred and a blood count shows a potential leukemia. The leukocytes number 22,000; lymphocytes are present in the proportion of more than 90 per cent, and there is moderate enlargement of the spleen. Thus study has to be made in any case of general exfoliative dermatitis to arrive at definite conclusions.

DR. M. J. REUTER, Milwaukee: I suggest as an aid to diagnosis in this case a therapeutic test with coal tar and ultraviolet radiation. If the condition is psoriasis a favorable response should be obtained with this regimen.

DR. MAURICE OPPENHEIM (by invitation): The patient has so many scales and such an erythematous condition that it is difficult to decide what kind of exfoliative dermatitis is present. One of the primary types of erythroderma exfoliativum is a premycotic stage of mycosis fungoides. Mycosis fungoides can start in this way. Lymphoblastoma and pityriasis rubra pilaris could be considered too. One way of deciding the diagnosis would be to find arsenic in the scales, if exfoliative dermatitis caused by chronic arsenical intoxication is present.

DR. CLARK W. FINNERUD: I have felt, as suggested by Dr. Senear, that the condition in this case is based on psoriasis, but apparently, according to the history, it was precipitated by arsenic.

Keratosis Follicularis (Darier) or Keratosis Follicularis Contagiosa (Brooke)? Presented by DR. N. C. BARWASSER (by invitation), Moline, Ill.

E. C., a white woman aged 24, states that the eruption appeared on the neck and face three months ago, accompanied by moderate itching, especially noted at night.

The past and family histories are irrelevant.

The eruption when first seen consisted of discrete, pea-sized dry reddish flat papules located especially on the sides of the neck and forehead. In about six weeks these papules became brownish and keratotic and appeared to heap up in the center. In some areas the papules became confluent. Later similar lesions appeared on the medial side of the forearms. The general behavior of this patient indicates some nervous instability.

Histologic examination of the specimen removed showed some areas of dyskeratosis, which evidently confirmed the diagnosis of Darier's disease. The blood count revealed 7,800 leukocytes with a normal differential count.

Treatment consisted of topical applications of astringent and antipruritic agents before the identity of the lesions became apparent.

DISCUSSION

DR. OLIVER S. ORMSBY: I should like to inquire whether or not other members of the family were affected. In view of the fact that no cases have been recorded for many years, I wondered why the Brooke type of keratosis follicularis was suggested in this case.

DR. MICHAEL H. EBERT: There are some associated observations in this case that were interesting from the point of view of avitaminosis. The patient's tongue is bright red and there are some patches, very much as one sees in anemia. If this condition were Darier's disease, I was not able to find the typical bodies in the section, though I have no doubt they were there. If the condition is Darier's disease it is the type that would respond rapidly to vitamin treatment.

Pseudoatrophoderma Colli. Presented by DR. EDWARD A. OLIVER and DR. IRVING A. LEWE (by invitation).

A. N., a white woman aged 39, complains of an asymptomatic eruption on the neck which first came to her attention two years ago, when her children remarked that her neck always appeared dirty. The eruption is persistent and shows no

change during menstrual periods. She has three children, none of whom are similarly affected, and she knows of no other members of her family with this condition.

The patient presents a faint macular eruption about the base of the neck. The macules are shiny and slightly discolored. The epidermis over the lesions is thrown up into tiny vertical folds which can be obliterated by stretching the skin. There are no lesions elsewhere on the body.

Histologic examination of the macules showed the following changes: The epidermis had more than the usual number of folds. The stratum corneum and the stratum granulosum were normal. The prickle cell layer was mildly acanthotic in some areas resulting in widened rete pegs and elongated papillae. In the papillary portion there was a moderate amount of round cell infiltration with few fibroblasts and some cellular and extracellular pigment. There was also a moderate infiltrate composed principally of round cells with a few fibroblasts about the blood vessels and pilosebaceous structures. The blood vessels were dilated.

In a section stained for elastic tissue by the Weigert method the elastic fibers were fragmented and thinned out. In a section stained by the Van Gieson method the collagen bundles were thickened.

DISCUSSION

DR. S. W. BECKER: This patient presents a clinical picture which Muir and I named. The change seems to be chiefly in the keratinization cycle. I suggest that she be treated with vitamin A, according to Peck's method of treating Darier's disease.

A Case for Diagnosis (Toxic Dermatitis?). Presented by DR. MINNIE O. PERLSTEIN.

Mrs. M., a Jewish housewife aged 40, gives a history of eruptions of two years' duration.

She states that blisters appeared in her mouth, coming on at intervals and disappearing spontaneously without scarring. At the time of appearance of the oral lesions crusted lesions developed on the scalp, which healed slowly. During the first year she had an occasional blister on the upper part of the chest, principally in the seborrheic areas. While in Florida during the winter of 1940 and for the following eight months she had no eruption either on the body or in the mouth. She spent the past winter in Florida and had no lesions of the skin, but immediately on returning to Chicago she began having lesions in the mouth and on the scalp and body. The oral lesions last from a few hours to a few days and are painful but do not interfere with eating. The lesions on the trunk are associated with and preceded by severe itching and, after rupture of the blisters, by burning. Three weeks ago, after the extraction of an infected tooth, she had an acute outbreak of numerous blisters on the back and upper part of the chest, a few on the upper part of the arms and a recurrence of lesions in the mouth. Most of these lesions have remained vesicular to date; a few have dried, and some are crusted. In addition, she presents an eruption on both forearms, more so on the right, of five years' duration, without remissions but at times with exacerbations. Her general health has been good.

The blood count and the urine were essentially normal.

The eruption consists of matchhead-sized to walnut-sized bullae, some tense walled, others flaccid, which are diffusely scattered over the back of the neck and shoulder. The majority of lesions are without inflammatory bases, but a number have an erythematous areola. The ruptured bullae leave a tender burning denuded epidermis which is covered by a thick grayish crust. The Nikolsky sign can be elicited some days and other days it cannot. There is a palm-sized plaque of edematous papules on the inner aspect of the right forearm with a smaller patch of similar lesions on the left forearm.

The histologic examination, as reported by Dr. Caro, revealed changes compatible with a diagnosis of toxic dermatitis.

DISCUSSION

DR. UDO WILE, Ann Arbor, Mich.: There are two or three things that come into the differential diagnosis, one of which is much more serious than any of the others. In view of the woman's race and the lesions in the mouth one is apt to think first of pemphigus, certainly not of a very acute type. I cannot believe that the condition in this case is pemphigus. The one small vesicular lesion that I saw on the back and the history fit in equally well with toxic erythema. I encounter many cases of pemphigus, and from time to time in cases of this type with lesions in the mouth there is response to treatment for toxic erythema. I think it is tremendously important not to mention the word pemphigus to the patient, whether the condition is well developed or not. Every one knows the psychic effect of the knowledge of fatal disease.

DR. OTTO H. FOERSTER, Milwaukee: I do not think it is possible to make a diagnosis at this time. Because of the background the condition may be a toxic erythema, though it may later be disclosed as pemphigus.

DR. MINNIE PERLSTEIN: In connection with the apprehension of patients, this woman has more than the usual amount because she has seen 2 members of her family—not blood relations, however—die of pemphigus. She is desperately afraid of pemphigus. As soon as the blisters appeared, she made the diagnosis. I personally feel the condition is not pemphigus.

I have used one method of treatment which I thought would be interesting from the standpoint of the record. At the time I first saw her she had heavy crusts. I gave her 30 per cent sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) in a water-soluble jelly (K-Y lubricating jelly), and in twenty-four hours the crusts were off. If I do not use it she has the crusts. Sulfathiazole will remove the crusts but it does not cure the condition.

The patient went to the Mayo Clinic, but the physicians there would not say whether the condition was or was not pemphigus. They did cutaneous tests and found she was sensitive to salmon, tuna fish and oats. She knows she can produce lesions in the mouth by eating food she is not supposed to eat. The lesions she presented in the mouth today came on at 2 o'clock following the eating of salmon at 11 o'clock. They are simple erosions and disappear in twenty-four to thirty-six hours. The lesions on the body give more trouble.

NOTE.—Since this patient was presented the eruption has spread to the sites of predilection of a dermatitis herpetiformis.

A Case for Diagnosis. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

Miss H. H., aged 22, has suffered from a dermatosis for sixteen months. The condition began with oozing and crusting lesions on the scalp and soon spread to the face, neck, axillas, groin and legs. At times groups of vesicles and pustules were present on the arms and forearms. Five months ago she was presented (report not published) at the clinical meeting of the Academy of Dermatology and Syphilology. Treatment by several physicians consisted of numerous local applications, roentgen ray therapy, administration of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) and injections of chaulmoogra oil and cobra venom.

On her admission to the hospital, two months ago, a psoriasiform dermatitis, partly diffuse and partly in patches, was present on the upper part of the trunk, the arms and the legs. On the scalp, the neck and the ears, in the axillas, on the breasts, in the groin, around the genitalia and in the gluteal folds the skin was erythematous and edematous; oozing and serous crusting were present.

The patient was hospitalized, and the following observations were made: On physical examination she was normal except for having small palpable lymph

nodes in the axillas and grains. The white blood count has varied from 6,500 to 10,200 and the eosinophil count from 9 to 12 per cent. The blood lipids amounted to 482 mg. per hundred cubic centimeters. The total nitrogen in the blood was 7.83 Gm. per liter. The nonprotein nitrogen content was 0.11 Gm. per liter. The protein content of the blood was 4.82 Gm. per hundred cubic centimeters. The albumin-globulin ratio was 1:00. The cholesterol, dextrose, serum calcium, serum phosphorus and serum chloride values were normal. The carbon dioxide value of the serum was slightly increased. The p_H of the serum was normal. The blood urea nitrogen amounted to 5.2 mg. per hundred cubic centimeters, and the urea clearance was normal. Ascorbic acid values varied from 0.2 to 1.14 mg. per hundred cubic centimeters. The basal metabolic rate was —3 per cent. Roentgenograms of the lungs and of the gastrointestinal tract were normal.

Treatment has consisted of high doses of ascorbic acid both by mouth and intravenously (about 575 mg. per day), sedation and various local applications. The dermatitis improved steadily except in the region of the scalp and ears, where it has resisted all local therapy.

During her stay in the hospital the diffuse psoriasiform dermatitis of the arms and legs cleared but was replaced by areas of distinct lichenification.

Histologic examination of a section from the left breast showed the stratum corneum to be hyperkeratotic and parakeratotic. The stratum mucosum was thickened, and the rete processes were elongated. The stratum mucosum was edematous, with the fluid chiefly intercellular. The papillae were edematous and contained an abundant infiltrate consisting chiefly of polymorphonuclear leukocytes. The infiltrate extended into the subpapillary layer of the cutis. The superficial blood vessels were dilated. The deeper portion of the dermis showed inflammatory reaction.

DISCUSSION

DR. MICHAEL H. EBERT: Was the diethylstilbestrol administered by mouth?

DR. M. E. OBERMAYER: It was not given by us.

DR. CLARK W. FINNERUD: I was of the impression that the condition might be a streptococcic eruption, the dermatitis possibly accentuated by the local treatment which had been employed.

DR. OLIVER S. ORMSBY: This patient was referred by Dr. Tobin to my clinic at the Academy meeting (report not published), and I presented her with the diagnosis of infectious dermatitis which possibly might later develop into pemphigus.

DR. JAMES H. MITCHELL: I have presented several patients before this society with scaling lesions throughout the scalp. One of them, about two years ago, had lesions in all of the folds of the body. I cleared her condition except for a discharging ear. Always she had streptococci present in the discharge. I think it would be well worth while to investigate for the presence of streptococci in this case.

DR. JAMES R. WEBSTER: When he sent the patient to Dr. Ormsby Dr. Tobin told me that he had used virtually all types of drugs recommended for the treatment of infectious dermatitis, including sulfanilamide and its derivatives, arsenic, quinine, potassium permanganate and gentian violet. All of these were ineffectual in modifying the course of the disease.

DR. M. E. OBERMAYER: We are grateful for your suggestions. We did not consider the possibility of an infectious type of dermatitis but thought the eruption was an example of that clinical entity which is difficult to classify because it exhibits some features of psoriasis, some of exudative neurodermatitis and some of so-called seborrheic eczema and which may change in aspect in the same patient from time to time and imitate any of the three dermatoses. In this case we favor the diagnosis exudative psoriasis because of the histologic picture, which, though not typical for psoriasis, is at least psoriasoid. The patients with this dermatosis have one feature in common, though the clinical picture may differ

considerably in each case, that is, their resistance to accepted methods of treatment for psoriasis, neurodermatitis or seborrheic eczema. This patient has been given lipocaic; so far no beneficial effect could be observed.

Pemphigus Vegetans: Continuous Treatment with Acetarsone. Presented by DR. MAURICE OPPENHEIM (by invitation) and DR. D. COHEN (by invitation).

P. G., a Jewish painter aged 42, married, entered Mount Sinai Hospital on Aug. 7, 1940, complaining of an eruption. Examination of the skin revealed various lesions all over the body, consisting of small pinhead-sized papules, vesicles and bullae, some the size of a quarter. Many oozing lesions with red angry wet bases were seen; others were confluent and irregular in outline. Some of the older lesions had large crusts. In the mouth, especially on the hard palate, there were many ruptured bullae. The history obtained at the hospital was that six weeks before entrance small vesicles appeared in both axillas. These lesions became larger and formed bullae, which later burst with subsequent crust formation. After this outbreak new lesions occurred and involved the scalp, face, neck, chest, back, upper extremities, groin and lower extremities. The patient complained of severe pruritus at the site of lesions at their onset.

The blood count and the urine were within normal limits. The Wassermann and Kahn reactions were negative. On August 9 there was 7.8 mg. of calcium per hundred cubic centimeters of blood and on August 24 11 mg.

Additional history revealed that this man suffered a burn on his right arm three or four months before the eruption appeared. This burn did not completely heal but always exhibited a few blisters.

The treatment consisted of six blood transfusions, one course of germanin, a high vitamin diet and continuous administration of acetarsone. He has taken 160 tablets (0.25 Gm. each) from August 1940 to May 1941.

Histologic examination revealed acanthosis, hyperkeratosis, formation of horny cysts in the epidermis and chronic inflammatory infiltration under the epidermis.

DISCUSSION

DR. A. W. STILLIANS: This patient was in my office in August 1940. At that time he had bullae in the mouth and both axillas and on the scalp, chest and back. There were some small vegetations in the axillas. I saw him only once and thought he had pemphigus.

DR. M. E. OBERMAYER: I hesitate to make suggestions to a colleague whose experience is far greater than mine, but there are two features in this case which make me feel that the diagnosis of pemphigus vegetans should be accepted with reservation. The patient was in a good state of health and stated that he has never felt sick during the course of the disease. Moreover, the dermatosis burned and itched severely. I wonder whether Dr. Oppenheim might not consider in diagnosis the rare, vegetative type of dermatitis herpetiformis.

DR. MAURICE OPPENHEIM (by invitation): In 1930 I published 4 cases of pemphigus chronicus treated with acetarsone (Ueber die Verwendung des Spirozids beim Pemphigus vulgaris chronicus und vegetans nebst Bemerkungen zur Spirozidtherapie, *Dermat. Wchnschr.* **91**:1855-1959, 1930). After my first presentation of such a case (Wiener dermatologische Gesellschaft, Sitzung vom 17. November 1927; abstracted, *Zentralbl. f. Haut-. u. Geschlechtskr.* **26**:350, 1928) several cases of pemphigus were published in which the condition was favorably influenced by acetarsone. Kromayer (*Deutsche med. Wchnschr.* **55**:229-230, 1929) reported 6 cases of pemphigus in which the condition healed(?). In 2 of these the condition was severe. Here the administration was over a long period with intermissions. In 1 case 600 tablets were given. All the patients improved so that they could return to their former occupation. The patient just presented is the same one presented by Dr. Ormsby at the meeting of the American Academy

of Dermatology in Chicago in December 1940. The patient entered the Mount Sinai Hospital in 1940 with the diagnosis of pemphigus vegetans. None of the dermatologists who saw him doubted this diagnosis. A definite improvement began after the administration of acetarsone. He has gained 30 pounds (13.5 Kg.) and has had no blister rash; the only signs of his disease are organized vegetations in both axillas and in the neck. The diagnosis was confirmed by the histologic picture. In this case the so-called primary lesion was in the right elbow joint, where the patient suffered a burn which did not heal. In every case of pemphigus vulgaris chronicus, particularly in pemphigus vegetans, one should try acetarsone.

DR. OTTO H. FOERSTER, Milwaukee: Pemphigus vegetans is an extremely rare disease in my experience; for many years the only undoubted case I had encountered was one in Dr. Neumann's clinic. Dr. Oppenheim's patient is one of the few fortunate ones who appears to have recovered. To that small list I can at least tentatively add another. The patient was a native-born farm woman of Swedish parentage, 32 years old, with the history of repeated attacks of "sore mouth and gums" for about one year. Shortly before her admission to the Wisconsin General Hospital there developed a rapidly extending eruption of flaccid coin-sized bullae on the trunk and extremities, many of which promptly formed papillomatous vegetations, along with condyloma-like lesions on the gums anteriorly and in the nail folds of the fingers and toes and vegetating lesions on the scalp. The formation of vegetating lesions of the nail folds at the onset or early in the course of the disease is said to be a characteristic feature of pemphigus vegetans. In the course of a few weeks, while the patient was treated with riboflavin, ascorbic acid and transfusions, the disease progressed steadily. Enormous vegetating masses formed in the inguinolabial and gluteal folds, in the axillas, beneath the breasts and to a lesser degree at the umbilicus, at the corners of the mouth, in the retroauricular folds and between the fingers and toes. The entire scalp was covered eventually by a turban-like vegetating mass with deep clefts. New bullae formed continuously on the trunk and extremities, and the general condition grew progressively worse. Metabolic studies by Dr. E. S. Gordon disclosed changes in the acid-base balance of the blood, which provided the indication for treatment with adrenal cortex extract and sodium chloride solution, as advocated recently by Talbott and Coombs (ARCH. DERMAT. & SYPH. **41**:359 [Feb.] 1940). In a short time after such treatment was begun the general condition improved, followed by improvement in the cutaneous lesions. Under this treatment, adjusted to variations in the chemical findings and continued for a period of months, the patient gradually recovered. Late in the course, after recovery was well under way, the remaining vegetative masses were treated with roentgen rays, which materially hastened their involution. Sulfathiazole (2-[para-aminobenzenesulfonamido]-thiazole) was given also for a short time preceding her discharge, and she has remained well to date without further treatment for three months. I do not doubt that in this extremely grave situation the treatment with adrenal cortex extract and sodium chloride solution correlated with adequate blood studies provided the means which led to recovery in this patient. As another therapeutic approach I think it is highly important that one keep in mind what Dr. Oppenheim has said about his experience with acetarsone.

Blastomycosis. Presented by DR. CLEVELAND WHITE.

A. L. M., aged 73, a former railway mail clerk, entered Passavant Memorial Hospital Sept. 20, 1940, complaining of swelling of the right foot, with discharge, which had been present since March 1940. There was no pain. The swelling was so pronounced that all the bony prominences were obliterated. He thought it was a recurrence of an inflammatory rheumatism which he had had seven years previously.

In his past history there were several illnesses: Tuberculous lymph glands were removed at the age of 28; he had erysipelas at the age of 43; cataracts were

removed from both eyes when he was 71. During the inflammatory rheumatism he had lesions on the posterolateral surface of the right thigh, which broke down. In his work he had traveled through Illinois, Wisconsin and Minnesota.

On physical examination his blood pressure was 170 systolic and 90 diastolic in the left arm and 160 systolic and 70 diastolic in the right arm. Inguinal lymph glands were slightly enlarged. On the posterolateral surface of the right thigh were two hyperpigmented areas, one the size of a silver dollar, which were former lesions that had healed with scar formation. There were ulcerations on the dorsum of the right foot midway between the toes and the ankle and between the second and fourth metatarsal bones. This area was depressed and covered with a crust. Swelling of the foot was present. There was no pitting on pressure. The circulation of the foot was impaired. The foot when dependent was violaceous and cold, and the skin was dry. The movements of the foot were impaired. Dermatophytosis was present. The skin of the body was of normal texture and pale, and there was no generalized eruption. There were senile angiomas, about ten on the back and eighteen on the chest and abdomen. There were multiple telangiectases on the medial margin of the right arm. Scars were present on the left side of the neck and in the left axilla.

A roentgenogram of the right leg and foot showed some generalized decalcification of the tibia and fibula but no evidence of bone destruction. The right foot showed definite evidence of periostitis involving the second, third and fourth metatarsal bones, particularly along the lateral surfaces. There was an area of destruction involving the distal half of the third cuneiform bone. There was little if any new bone formation.

A stereoscopic roentgenogram of the chest revealed obliteration of the right costophrenic angle by adhesions, thickening of the apical pleura of the right side, mottling of the apex of the left lung and a band of density extending vertically in the upper third of the left lung. The lungs appeared to be emphysematous. The heart was normal in size and position. Deposits of calcium were present in the wall of the arch of the aorta. The ribs showed advanced calcification of cartilage.

Histologic examination of a specimen from the dorsum of the right foot showed the presence of doubly refractile bodies containing what were apparently endospores. The diagnosis was coccidioidal granuloma or blastomycosis. This diagnosis was confirmed by Dr. E. F. Hirsch, of St. Luke's Hospital, and Dr. McKnight of Leland Stanford University, to whom the sections were sent.

Smears and cultures of pus from the foot were negative after five weeks' incubation on Sabouraud's medium. In the smear of the sputum no structures were found which resembled Coccidioides. Culture was negative for Coccidioides, only gram-positive and negative cocci being present. Cultures showed Staphylococcus albus, a hemolytic streptococcus and Micrococcus catarrhalis.

A guinea pig was inoculated, and an abscess developed at the site of inoculation. Smears with 30 per cent sodium hydroxide showed no evidence of coccidioides.

Complement fixation and precipitation tests sent to Duke and Leland Stanford universities were reported negative for Coccidioides immitis. The Kahn reaction was negative. Examination of the blood and urinalysis gave negative results.

A section was sent to Dr. Weidman, who reported that in his opinion the condition was atypical American blastomycosis. In the presence of such typical structures in the section it was difficult for him to understand the failure to secure a culture.

DISCUSSION

DR. CLEVELAND WHITE: I was unable to culture the organism. I observed another case recently in which the histologic picture was the same. I sent a section to Dr. Weidmann, and again he said he did not see why I could not secure a culture.

Pityriasis Rubra Pilaris. Presented by DR. A. W. STILLIANS and DR. E. M. SMITH JR. (by invitation).

A white woman aged 38 states that the present eruption started six weeks ago as a redness on the back of the hands and in the posterior axillary folds. One week later the redness appeared on her face. Itching was present on irritation only. She states that she has had a dry eczema every winter since childhood. It improves during the summer. Menses have always been normal, but at such times her eruption is expected to become worse. At the age of 13 she had to remain out of school for one year because of the extensive eczema. The palms and soles have remained uninvolved.

On examination there is a symmetric maculopapular eruption involving the midline of the face, the dorsa of the hands and wrists, the extensor surfaces of the forearms and the posterior axillary folds. There are lichen-planus-like lesions on the shoulder and follicular spines on the lesions on the forearms.

The patient is now six months pregnant. She has two children whose health and skin are normal.

Examination of the blood revealed 12,100 leukocytes with a normal differential count, 4,920,000 erythrocytes and 72 per cent hemoglobin. The urine was normal.

DISCUSSION

DR. CLARK W. FINNERUD: I saw the patient in 1928, and several of the members have seen her on previous occasions. She was one of 2 patients to whom I referred several times, as has Dr. Ebert, as having been completely freed of pityriasis rubra pilaris by taking liberal doses of thyroid. When I saw her the first time her basal metabolic rate was —21.8 per cent. That was in September 1928. She took 6 grains (0.4 Gm.) of thyroid daily, and the condition cleared entirely in a few months. A year or two later she had a recurrence, which also cleared with thyroid medication.

DR. A. W. STILLIANS: Our interest was aroused because the present attack came on during pregnancy and because of the lichen-planus-like lesion.

Naevus Striatus Symmetricus of the Thumbs. Presented by DR. MAURICE OPPENHEIM (by invitation) and DR. D. COHEN (by invitation).

Mrs. A. K., a white woman aged 38, presents a condition of her thumb nails which has been present since birth. There are no subjective symptoms. In the center of the nails there are linear areas measuring 3 mm. wide and 13 mm. long. These areas are composed of parallel short dark lines which extend from the posterior nail fold to the free end of the nail and are depressed in regard to the nail surface. There are no signs of inflammation, and the other nails are normal.

This condition is not present in any of the patient's children or in her parents.

DISCUSSION

DR. J. E. GINSBERG: I questioned the patient and could not confirm the implication that the condition has been present since birth. The woman said she remembered having had it since childhood. I believe it is symmetric traumatic onychia. I had a patient several months ago who had a similar condition. She had a habit of pushing back the thumb nail cuticle with a nail of the opposite hand. When she discontinued this habit the lesions healed.

DR. MAURICE OPPENHEIM (by invitation): The lesion looks much too regular and too symmetric to be made by trauma by pushing back the cuticle with the nail. I am familiar with nail traumas in connection with my study of occupational diseases of the skin, and I have never encountered a similar case. Whether it is possible to produce artificially such regular striations I do not know. Heller (Die Krankheiten der Nägel, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 13, pt. 2) mentioned traumatic nail conditions, but he did not mention such a condition as this.

Book Reviews

The Biologic Fundamentals of Radiation Therapy. A Textbook. By Dr. Friedrich Ellinger, Research Fellow, Radiotherapy Department, Montefiore Hospital, New York. Formerly Privatdozent in Radiology of the University of Berlin. With a preface by Maurice Lenz, M.D., Associate Clinical Professor of Radiology, Columbia University, Director of City Cancer Hospital, Chief of Radiotherapy Departments Presbyterian Hospital and Montefiore Hospital, New York. English translation by Reuben Gross, M.D., formerly Resident Physician, Radiotherapy Department, Montefiore Hospital, New York, First Lieut. M. C., U. S. A. Price, $5.00. Pp. 360, with 141 illustrations. New York: Nordemann Publishing Company, Inc, 1941.

The author has undertaken a colossal task. The material contained in the book is so extensive that it had to be presented in catalog form. Statements are made, and the authorities for these statements are cited. Whether or not the statemens are true is not adequately discussed. The result is that the reader is left confused. The space allotted to the bibliography is out of proportion to the rest of the book; there are 360 pages, 47 of which are devoted to the bibliography. The author and subject indexes cover an additional 17 pages.

The book is divided into five parts. The first part deals with the action of roentgen rays and the gamma radiations of radium, the second with corpuscular rays, the third with ultraviolet rays, the fourth with further concepts of light and the fifth with general radiation biology and therapy. It can be seen at a glance that the various forms of radiant energy and the various conditions for which this energy is employed are included.

The approach is novel in that the author compares roentgen therapy to pharmacology. The book cannot be used as a text for treating cutaneous diseases with the various sources of radiation but does serve as an excellent manual for reviewing the biologic action of therapeutic radiations on the various organs and systems. The text is full of references so that the reader may readily refer to original sources. It was disappointing to the reviewer to find that few American and English works were consulted, or if they were the material does not appear in the text or in the long bibliographic list.

The printing and paper are good. The illustrations for the most part are fair, though some are poor. Many of them are copies from previously published articles. The reviewer thinks the title on the cover is misleading. One would assume that the title "Radiation Therapy" means that the book is one which deals with the details of treating various diseases with radiant energy. Some of the therapeutic suggestions and data do not conform with those which are generally accepted in the United States. For example, in a table on page 15 the erythema dose for unfiltered soft rays is given as 450 r. Most dermatologists employ 300 r, measured in air, on a field of 1 inch (2.5 cm.) square as the erythema dose. There are many other things similar to this throughout the book which are questionable.

The author is certainly to be congratulated on being able to condense such an enormous amount of material in a small volume. When one reads the book one is stimulated to inquire further into the many mysteries of the biologic actions produced by different radiations.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago
Paul A. O'Leary, Secretary-General, 102-2d Ave. S. W., Rochester, Minn.
Place: New York. Time: Postponed indefinitely.

Pan American Medical Association, Section of Dermatology and Syphilology

Austin W. Cheever, Secretary, 464 Beacon St., Boston.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

B. Usher, President, 1538 Sherbrooke St. W., Montreal.
Frederick Kalz, Secretary-Treasurer, 1414 Drummond St., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1, England.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1, England.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

C. F. Lehmann, Chairman, 705 E. Houston St., San Antonio, Texas.
Nelson P. Anderson, Secretary, 2007 Wilshire Blvd., Los Angeles
Place: Atlantic City. Time: June 8-12, 1942.

American Academy of Dermatology and Syphilology

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary-Treasurer, 416 Marlborough St., Boston.

American Dermatological Association

William H. Guy, President, 500 Penn Ave., Pittsburgh.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.

Society for Investigative Dermatology

Bedford Shelmire, President, 1719 Pacific Ave., Dallas, Texas.
S. W. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.
Place: Cleveland.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

Lawrence C. Goldberg, Secretary-Treasurer, 623 Doctors Bldg., Cincinnati.

Mississippi Valley Dermatological Society

Lawrence C. Goldberg, Secretary-Treasurer, 623 Doctors Bldg., Cincinnati.
Place: Chicago.

New England Dermatological Society

John G. Downing, President, 520 Commonwealth Ave., Boston.
Francis M. Thurmon, Secretary, 520 Commonwealth Ave., Boston.

Northern New Jersey Dermatological Society

S. Oleynick, President, 31 Lincoln Pk., Newark.
C. C. Carpenter, Secretary, 129 Summit Ave., Summit.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

Howard King, Chairman, 328 Doctors Bldg., Nashville, Tenn.
J. Lamar Callaway, Secretary, Duke Hospital, Durham, N. C.

Southern Medical Association, Section on Dermatology and Syphilology

Howard Hailey, Chairman, 107 Doctors Bldg., Atlanta, Ga.
John H. Lamb, Secretary, 117 N. Broadway, Oklahoma City.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

H. J. Templeton, Chairman, 3115 Webster St., Oakland.
Frances Torrey, Secretary, 123 Pemberton Pl., San Francisco.

Connecticut State Medical Society, Section on Dermatology

Ralph E. McDonnell, Chairman, 158 Whitney Ave., New Haven.
Louis O'Brasky, Secretary, 1172 Chapel St., New Haven.

Florida Society of Dermatology and Syphilology

Wiley M. Sams, Chairman, 25 S. E. 2d Ave., Miami.
Lauren M. Sompayrac, Secretary, 117 W. Duval St., Jacksonville.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

William Boardman, President, 388 Marlborough St., Boston.
J. H. Swartz, Secretary, 371 Commonwealth Ave., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

H. Bauckus, Chairman, 89 Bryant St., Buffalo.
Eugene Traub, Secretary, 140 E. 54th St., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON DERMATOLOGY

Paul A. Deckard, Chairman, 814 N. 2d St., Harrisburg.
Bernhard A. Goldmann, Secretary, 500 Penn Ave., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Frank Menaugh, Chairman, Ford Hospital, Detroit.
Eugene A. Hand, Secretary, 801 Second National Bank Bldg., Saginaw.

MINNESOTA DERMATOLOGICAL SOCIETY

H. E. Michelson, President, 825 Nicollet Ave., Minneapolis.
F. W. Lynch, Secretary-Treasurer, 317 Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

John H. Lamb Jr., President, 117 N. Broadway, Oklahoma City.
Onis G. Hazel, Secretary, 1200 N. Walker, Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

Arthur Schoch, President, 1719 Pacific Ave., Dallas.
Duncan O. Poth, Secretary-Treasurer, 414 Navarro St., San Antonio.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Russell J. Fields, Chairman, 1726 I St. N. W., Washington, D. C.
Maurice Sullivan, Secretary-Treasurer, 11 E. Chase St., Baltimore.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Van Alstyne H. Cornell, President, 40 E. 61st St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.
Time: Fourth Thursday of each month from October to May, inclusive.

BROOKLYN DERMATOLOGICAL SOCIETY

S. H. Silvers, President, 920 Bushwick Ave., Brooklyn.
M. Estrin, Secretary, 61 Eastern Parkway, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Edwin D. Putnam, President, 201 N. Union St., Olean, N. Y.
James W. Jordon, Secretary, 471 Delaware Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Leon H. Griggs, President, 1804 State Tower Bldg., Syracuse.
Maxwell C. Snider, Secretary, 106 Oak St., Binghamton.

CHICAGO DERMATOLOGICAL SOCIETY

Leonard F. Weber, President, 7 W. Madison St., Chicago.
Michael H. Ebert, Secretary-Treasurer, 25 E. Washington St., Chicago.

CINCINNATI SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

Harry L. Claasen, President, Provident Bank Bldg., Cincinnati.
Lawrence C. Goldberg, Secretary-Treasurer, 623 Doctors Bldg., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except July, August and September.

Cleveland Dermatological Society

Harold N. Cole, President, 1422 Euclid Ave., Cleveland.
Charles G. La Rocco, Secretary, 669 Rose Bldg., Cleveland.

Detroit Dermatological Society

John H. Cobane, President, 10 Peterboro Ave., Detroit.
John H. Besancon, Secretary-Treasurer, 1510 Eaton Tower, Detroit.

Kansas City (Mo.) Dermatological Society

C. C. Dennie, President, 1103 Grand Ave., Kansas City.
Thomas B. Hall, Secretary, 902 Professional Bldg., Kansas City.

Los Angeles Dermatological Society

Harry C. Lindsay, President, 595 E. Colorado St., Pasadena, Calif.
Saul S. Robinson, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

J. Frank Fraser, Chairman, 115 E. 61st St., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.

Montreal Dermatological Society

L. P. Ereaux, President, 1390 Sherbrooke St. W., Montreal, Canada.
Paul Poirier, Secretary, 456 Sherbrooke St. E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Louis Tulipan, Chairman, 50 Park Ave., New York.
Timothy J. Riordan, Secretary, 136 E. 64th St., New York.

New York Dermatological Society

Edward R. Maloney, President, 136 E. 64th St., New York.
J. Gardner Hopkins, Secretary-Treasurer, 630 W. 168th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln, Neb.

Philadelphia Dermatological Society

A. Strauss, Chairman, 136 S. 16th St., Philadelphia.
Donald M. Pillsbury, Secretary, 133 S. 36th St., Philadelphia.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

M. W. Rubinstein, President, Medical Bldg., Pittsburgh.
M. F. Pettler, Secretary, 1319–8th Ave., Beaver Falls, Pa.
Time: Third Thursday of every month except July and August.

St. Louis Dermatological Society

Norman Tobias, President, Missouri Theatre Bldg., St. Louis.
Joseph Grindon Jr., Secretary-Treasurer, 323 Lister Bldg., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

Arne E. Ingels, President, 490 Post St., San Francisco.
Ervin Epstein, Secretary-Treasurer, 1904 Franklin St., Oakland, Calif.
Time: Third Friday of February, April, September and November.